THE GEORGE BLUMER
EDITION OF
BILLINGS-FORCHHEIMER'S
THERAPEUSIS OF INTERNAL DISEASES

VOLUME IV

THE GEORGE BLUMER EDITION OF BILLINGS-FORCHHEIMER'S THERAPEUSIS OF INTERNAL DISEASES

CARE AND MANAGEMENT OF MALADIES AND AILMENTS OTHER THAN SURGICAL

VOLUME IV

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EDITED BY

GEORGE BLUMER, M.A. (YALE), M.D.

DAVID P. SMITH CLINICAL PROFESSOR OF MEDICINE, YALE UNIVERSITY SCHOOL OF MEDICINE, ATTENDING PHYSICIAN TO THE NEW HAVEN HOSPITAL

FORMER EDITORS

FREDERICK FORCHHEIMER, SC.D. (HARV.), M.D.

FORMERLY PROFESSOR OF MEDICINE, MEDICAL DEPARTMENT, UNIVERSITY OF CINCINNATI (OHIO-MIAMI MEDICAL COLLEGE), PHYSICIAN TO CINCINNATI HOSPITAL

FRANK BILLINGS, SC.D. (HARV.), M.D.

PROFESSOR OF MEDICINE, UNIVERSITY OF CHICAGO AND RUSH MEDICAL COLLEGE, CHICAGO

ERNEST E. IRONS, PH.D., M.D.

CLINICAL PROFESSOR OF MEDICINE, RUSH MEDICAL COLLEGE, CHICAGO

CONTRIBUTORS TO VOLUME IV

WILLIAM NATHANIEL BERKELEY, A.B., B.Ph., M.D.
Formerly Attending Physician at the Good Samaritan Dispensary, and formerly Director of the Laboratory of Experimental Medicine, Cornell Medical College

Diseases of the Parathyroid Glands, Diseases of the Pituitary Gland, Diseases of the Pineal Gland

HENRY WALD BETTMAN, B.L., M.D.
Associate Professor of Medicine, College of Medicine, University of Cincinnati

Diseases of the Intestines, Diseases of the Liver

FRANK BILLINGS, M.D., Sc.D.
Professor of Medicine, University of Chicago and Rush Medical College, Dean of Faculty, Rush Medical College, Consulting Physician Presbyterian Hospital, Chicago

Arthritis Deformans

KENNETH D. BLACKFAN, M.D.
Professor of Pediatrics at Harvard Medical College and Director in Charge of the Infants and Children's Hospital at Boston

Diseases of the Thymus Gland

GEORGE BLUMER, A.B., M.D.
David P. Smith Clinical Professor of Medicine, Yale University School of Medicine, Attending Physician to the New Haven Hospital

Visceral Manifestations of Erythema Multiforme, Diseases of the Adrenals, Developmental Diseases, Hæmochromatosis, Diseases of the Spleen

ERNST P. BOAS, A.M., M.D.
Medical Director, Montefiore Hospital

Diseases of the Thyroid Gland

SAMUEL T. DARLING, M.D., D.Sc.
Director, Station for Field Studies in Malaria, International Health Board; Formerly Chairman, Uncinariasis Commission to the Orient, International Health Board

Epidemic Dropsy

OTTO H. FOERSTER, M.D.
Dermatologist to the Hospital of the University of Wisconsin; Head of the Department of Dermatology of Columbia Hospital, Milwaukee Hospital, Milwaukee Infants' Hospital, Milwaukee Children's Hospital

Diseases of the Mouth

FREDERICK FORCHHEIMER, M.D., Sc.D.
Formerly Professor of Medicine, Medical Department of the University of Cincinnati (Ohio-Miami Medical College), Physician to Cincinnati Hospital

Diseases of the Adrenals

THOMAS B. FUTCHER, M.B.
Associate Professor Clinical Medicine, Johns Hopkins University, Assistant Visiting Physician, Johns Hopkins Hospital

Alkaptonuria and Ochronosis, Lithuria, Indicanuria, Pentosuria, Oxaluria, Phosphaturia

A. GALAMBOS, M.D.
Clinical Assistant to Post-Graduate Hospital and Medical School and Mount Sinai Hospital; Formerly Associate in Medicine in University Clinic of Professor A. Koranyi, in Budapest

Diseases of the Stomach

HENRY J. GERSTENBERGER, M.D.
Professor of Pediatrics, Medical School of Western Reserve University; Medical Director Babies' Dispensary and Hospital of Cleveland

Scurvy

ERWIN G. GROSS, B.S., M.S., Ph.D.
Instructor Department of Pharmacology and Toxicology, Yale Medical School

Obesity

JOHN T. HALSEY, M.D.
Professor of Pharmacology and Therapeutics, Tulane University of Louisiana, Attending Physician Charity Hospital, New Orleans

Diseases of the Peritoneum

CAMPBELL P. HOWARD, A.B., M.D., C.M.
Professor of Theory and Practice of Medicine, State University of Iowa, College of Medicine, Physician to the University Hospital, State University of Iowa

Diseases of the Salivary Glands, Diseases of the Lymph Nodes

JACOB KAUFMANN, M.D.
Professor of Clinical Medicine, College of Physicians and Surgeons, Columbia University, Attending Physician Lenox Hill Hospital, New York

Diseases of the Stomach

EDWIN A. LOCKE, Ph.B., A.M., M.D.
Clinical Professor of Medicine, Harvard Medical School, Visiting Physician, Boston City Hospital, Chief of Staff, Boston Sanatorium

Obesity

GEORGE M. MACKENZIE, A.B., M.D.
Assistant Professor of Medicine, Columbia University, College of Physicians and Surgeons, Associate Visiting Physician, Presbyterian Hospital, New York

Serum Disease

DAVID MARINE, A.M., M.D.
Director of Laboratories, Montefiore Hospital, Assistant Professor Pathology, Columbia University

Diseases of the Thyroid Gland

C. F. MARTIN, B.A., M.D., C.M.
Dean of Faculty, Professor of Medicine, McGill University, Physician-in-Chief, Royal Victoria Hospital, Montreal

The Anemias, Leukemia and Hodgkin's Disease, Erythremia and Polycythemia, Hemorrhagic Diseases

JOSEPH HERSEY PRATT, A.M., M.D.
Boston, Massachusetts

Gout

GEORGE ELMER SHAMBAUGH, Ph.B., M.D.
Clinical Professor of Otology and Laryngology, University of Chicago, Chairman of Department of Otolaryngology, Rush Medical College, Otologist and Laryngologist at Presbyterian Hospital, Chicago

Diseases of the Pharynx

P. G. SHIPLEY, M.D.
Instructor in Pediatrics, Johns Hopkins University, Assistant Dispensary Pediatrist, Johns Hopkins Hospital

Rickets

BURT RUSSELL SHURLY, B.S., M.D., F.A.C.S.
Professor of Laryngology and Otology, Detroit College of Medicine, Chief of Staff and Teaching Clinic, Detroit Eye, Ear, Nose and Throat Hospital, Consulting Laryngologist, Harper Hospital

Diseases of the Pharynx

BERTRAM WELTON SIPPY, M.D.
Professor of Medicine, University of Chicago

Diseases of the Esophagus

WALTER R. STEINER, A.M., M.D.
Visiting Physician at the Hartford Hospital, Consulting Physician at the New Britain General Hospital

Vasomotor and Trophic Diseases

KURT H. THOMA, D.M.D.
Assistant Professor of Oral Histology and Pathology and Member of the Research Committee of Harvard University Dental School

Diseases of the Teeth

WILDER TILESTON, A.B., M.D.
Clinical Professor of Medicine, Yale University, Visiting Physician, New Haven Hospital

Hemolytic Jaundice

WALTER TIMME, B.S., M.D.
Professor of Neurology, Polyclinic Medical School and Hospital, Professor of Endocrinology, Broad Street Hospital, Attending Neurologist, Neurological Institute, New York

Diseases of the Gonads, Polyglandular Syndromes

I. CHANDLER WALKER, A.B., M.D.
Associate in Medicine, Peter Bent Brigham Hospital; Assistant in Medicine, Harvard Medical School

Hay Fever, Bronchial Asthma, Anaphylactic Food Poisoning

H. GIDEON WELLS, Ph.B., A.M., Ph.D., M.D.
Professor of Pathology in the University of Chicago and Rush Medical College, Director of Medical Research, Otho S. A. Sprague Memorial Institute, Attending Pathologist, Cook County and Central Hospitals, Chicago

Beri-Beri and Nutritional Edema

EDWARD J. WOOD, B.Sc., M.D., D.T.M. (Eng.)
Consulting Physician to the James Walker Memorial Hospital, Wilmington, and the State Hospital, Raleigh

Pellagra

R. T. WOODYATT, M.D.
Clinical Professor in the Department of Medicine, University of Chicago, Attending Physician Presbyterian Hospital, Chicago, Director, Otho S. A. Sprague Memorial Institute Laboratory for Clinical Research

Diabetes Mellitus, Renal Diabetes

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DISEASES ASSOCIATED WITH ANAPHYLAXIS

CHAPTER I

HAY-FEVER

I. Chandler Walker

In 1819 John Bostock recognized that certain individuals were attacked during the summer season with a condition which he named hay-fever and which is described as watering and itching of the eyes and nose, sneezing, and itching of the throat. We now know that not only does this condition attack an individual at definite seasons of the year, when it is called seasonal hay-fever, but also it may be present more or less continually throughout the entire year in which case it is called perennial hay-fever. Furthermore we now recognize a pseudo-hay-fever and since, in some instances, vasomotor rhinitis is very difficult to differentiate from perennial hay-fever, it may be proper to include vasomotor rhinitis in this group.

Seasonal Hay-fever.—For convenience seasonal hay-fever is divided into three groups, namely, spring, summer and autumn. The spring type concerns those who have symptoms during February, March, April and May and the causative agent is usually the pollens of trees. The summer type concerns those who have symptoms during late May, June and July and the causative agent is usually the pollens of the grasses. The autumn type concerns those who have symptoms during August and September and the causative agent is usually the pollen of ragweed—dwarf ragweed in the East and giant ragweed in the West. Naturally the season of pollination of these various plants varies according to the location; however, the history of the patient will indicate the time of year when symptoms are present so that cutaneous tests may be done with the pollens prevalent at that time.

Tree Pollen Hay-fever.—The first pollen season begins in February and continues into May, during which time various trees pollinate. Since the season of pollination of the individual trees continues only from a few days to two weeks at the most, it does not seem essential that treatment be given. However, treatment may be successfully given for tree pollens in

the same manner as for other pollens for which treatment will be detailed later on.

Summer Type of Hay-fever.—Patients who have hay-fever during May, June and July, the so-called rose cold period, are exposed to many kinds of pollens; however, the cause of hay-fever at this time is practically limited to the pollens of the grass family. Lawn grass is probably rarely, if ever, the chief cause of hay-fever. Since corn is a member of the grass family, and since the table variety pollinates during July, it must be considered among the possible causes of early hay-fever; however, intimate exposure is required to produce symptoms. The same is likewise true of wheat, oats, barley and rye.

The grasses, then, with which we are concerned in New England are June grass, timothy and redtop, the pollens of which are light and are carried by wind considerable distances. June grass begins to pollinate some years as early as the middle of May and pollination continues for about three weeks. Timothy and redtop begin to pollinate between the middle of June and the first of July, depending on the season, and pollination continues until the middle or last of July; usually, the season of pollination lasts about six weeks. In the Southwest (Watson) the following must be considered instead of the above grasses: blue grass, Bermuda grass, Johnson grass, broom grass, stink grass and spear grass; alfalfa is also a common cause; in California (Hall) similar grasses as well as others cause hay-fever.

Autumnal or Late Hay-fever.—In the New England states, most of the compositæ, such as ragweed, golden rod, sunflower, golden glow and aster, pollinate during August and September; however, pollens other than dwarf ragweed rarely, if ever, are the chief cause of symptoms during the late hay-fever season. In the West giant ragweed is more prevalent than dwarf ragweed and in the Southwest (Watson) false ragweed, rabbit brush, and sagebrush are important causes; in California (Hall) the pollens are similar.

The pollens that may be the possible cause of hay-fever at various seasons have been outlined and the cutaneous test, which when used with these pollens will determine the probable cause, has been described in the chapter on Bronchial Asthma. Before treatment is given it is essential to do cutaneous tests with various dilutions of the pollens or pollen proteins in order to determine to which pollen of several the patient is most sensitive and with which pollen the patient should be treated, and with what dilution of the pollen treatment should be begun. Treatment should not be given with a dilution of pollen that gives a reaction on the skin, but should be begun with the strongest solution that fails to give any reaction whatever.

TREATMENT AND TEST SOLUTIONS

These solutions may be made as follows: To 0.5 gm. of the dry pollen is added 44 c.c. of sterile physiologic sodium chlorid solution, and the mixture is shaken thoroughly at frequent intervals for twenty-four hours, after which enough absolute alcohol (6 c.c.) is added to the mixture to make the alcoholic content 12 per cent. Again, the mixture is thoroughly shaken at frequent intervals for twenty-four hours, after which it is centrifugalized at high speed and the supernatant fluid is pipetted off and saved. This supernatant fluid, therefore, consists of the pollen protein dissolved in a 12 per cent alcoholic physiologic sodium chlorid solution and it represents, by weight, 1 part pollen to 100 parts solvent. This 1:100 solution is used as stock, and from it other dilutions, 1:500, 1:1,000, 1:5,000 and 1:10,000 are made, using a 12 per cent alcoholic physiologic sodium chlorid solution as a diluent. These solutions are used not only for the skin tests but for treatment, and with the addition of a small crystal of thymol they keep for many months in a cool place; by the addition of carbolic acid to a 0.5 per cent content the solutions are rendered sterile.

Method of Treating Preseasonally with Pollen Extracts.—The first treatment consists of from 0.1 to 0.2 c.c. of that dilution next higher than the one which gave a positive skin test, or, in other words, the first dose is 0.1 c.c. or 0.2 c.c. of the strongest dilution which failed to give any skin reaction whatever, no matter how slight. With my pollen extracts, made as above described, the majority of patients will give a more or less positive reaction with the 1:10,000 dilution; therefore, the first treatment should be 0.1 c.c. or 0.2 c.c. of the 1:20,000 dilution. Treatments are given subcutaneously once a week, and each week the amount of the extract is gradually increased, so that, as the treatment progresses, stronger and stronger dilutions are used, until one or more doses of the 1:100 dilution are given. As an example, the following is a desirable outline of treatment for a patient who gives a more or less positive skin test with a 1:5,000 dilution of pollen extract; 1:10,000 gives 0.15 c.c.; 1:5,000 gives 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1:1,000 gives 0.15 c.c., 0.25 c.c.; 1:500 gives 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1:100 gives 0.15 c.c., 0.2 c.c., 0.25 c.c. Each dose is given preferably at weekly intervals and never oftener than once every five days.

The usual schedule of treatment calls for fourteen inoculations; however, for some reason or other, modifications frequently have to be used. Often a patient is so sensitive to the pollen that a 1:10,000 dilution gives a slight reaction, thus necessitating an initial dose of 0.15 c.c. of a 1:20,000 followed by possibly two doses of 1:10,000. Often it happens that a patient has considerable local or general reaction following some one treatment in the schedule, thus necessitating the repetition of that

particular dose before the next increase is given. More often the patient presents himself for treatment too late to complete the scheduled series of treatments before the onset of pollination so that, for preseasonal treatment alone, some of the final treatments in the schedule must be omitted. This schedule is often modified purposely with certain individual cases. For instance, in some cases the second treatment with the 1 : 1,000 dilution, namely, 0.25 c.c., is omitted, and in some cases instead of giving 0.15 c.c. of the 1 : 100 dilution, when this happens to be the final treatment that the patient is to receive because of onset of pollination, a fifth treatment with the 1 : 500 dilution, namely, 0.55 c.c., is often substituted, and even a sixth treatment with the 1 : 500 dilution, namely, 0.65 c.c., is sometimes given. These larger doses of 1 : 500 approximate the amount of protein in 0.15 c.c. and 0.2 c.c. of the 1 : 100 dilution; therefore the fifth and sixth treatment with the 1 : 500 dilution, as outlined, is practically the equivalent of giving 0.15 c.c. and 0.2 c.c of the 1 : 100 dilution. Since by far the great majority of patients are treated from three to five times with the 1 : 500 dilution, and since this number of treatments has given fairly satisfactory results, this number of treatments, which consists usually of a total of ten, may be considered as worth giving, although a continuance of the schedule beyond three doses of the 1 : 500 dilution is most desirable, and giving less than three treatments with the 1 : 500 dilution is undesirable.

Since the majority of autumnal hay-fever patients have their first symptoms between August 10 and 20, during which time the compositæ, chiefly ragweed, begin to pollinate, in order to complete the above schedule just previous to the onset of symptoms and pollination, patients must begin treatment between the last week in April and the first two weeks in May. Beginning treatment the first week in June permits of giving from three to five treatments with the 1 : 500 dilution. Likewise, since the early type of hay-fever, or so-called rose cold, which is usually caused by the grasses, begins in May, treatment for this type of hay-fever should begin previous to the first of March, and the starting of treatment as late as the first of April will not permit of more than from three to four treatments with the 1 : 500 dilution, according to the schedule outlined. Naturally, in various localities, these seasons differ, and consequently the beginning of treatment must vary.

During-the-Season or Curative Treatment with Pollen.—Frequently patients present themselves for treatment during their hay-fever attack, and although pollen treatment at this time does not seem to be very logical on the basis of anaphylaxis, the patient often will insist on taking the chance. Pollen treatment during the season does not seem logical because the patient is being injected with the pollen which is causing symptoms at the same time that he is being exposed to the pollen present in the air which he is inhaling. The danger resulting from large doses of the in-

jected pollen is obvious because of an overdose, due to the combination of the injected pollen and the inhaled pollen. Therefore, in order that during-the-season treatment should be beneficial, the patient must be injected with minute amounts of the pollen extract in order to diminish artificially a few of the patient's antibodies, thus leaving a smaller number of antibodies in the patient for combination with the pollen antigen that is inhaled. If too much pollen extract (antigen) is injected, the patient should have symptoms due to overtreatment alone, or he should be made worse, due to the injection of pollen extract (antigen) superimposed on the inhalation of pollen (antigen). It is evident that on the basis of anaphylaxis during-the-season treatment is hazardous, and, although the skin test is the best guide as to the proper treatment, there is no way of obtaining an estimate of or controlling the amount of pollen that the patient may inhale.

Preceding and During-the-Season Treatment with Pollens.—Some patients present themselves a few weeks previous to their season of symptoms, that is, they apply for treatment too late for preseasonal treatment alone and too early for during-the-season treatment. Rather than let them wait until their symptoms begin and then give them during-the-season treatment, it is best to begin treatment immediately and continue the treatment on through their period of symptoms. This method of treatment yields better results than does the during-the-season treatment, but not as good results as the preseasonal treatment.

During-the-Season Treatment with Bacteria.—Occasionally when preseasonal pollen treatment fails, treatment during the season with autogenous nasal vaccine or a mixed streptococcus vaccine will benefit. The reason for such treatment is that it is quite possible that ragweed pollen exposure may in some cases cause such a severe irritation of the mucous membranes that ever-present bacteria may, either alone or together with ragweed pollen, be a cause of hay-fever symptoms.

The permanency of benefit from treatment seems to depend largely upon the individual and to some extent upon a large amount of treatment which renders the patient non-sensitive. After two or three years of consecutive treatment the majority of patients will continue free or practically free from symptoms for another two or three years without treatment; after this period of time symptoms return more or less gradually. Occasionally a patient will be free only one year before symptoms return and occasionally symptoms will be as severe the first year that treatment is omitted. Rarely one season's treatment will protect for several years and I think treatment every other year with some individuals will keep the patient quite free from symptoms. As a rule I feel it best to give two or three successive years' treatment before permitting omission of treatment.

Miscellaneous Treatment.—For those hay-fever patients who cannot be treated as already outlined or in whom the pollen treatment fails, a

change of locality to a place where the causative pollen does not grow is advisable. High altitudes are usually free from causative pollens and naturally ocean trips will avoid pollens. When avoidance of the pollens is out of the question as well as desirable treatment, dark glasses, a boric acid eye wash, adrenalin nasal sprays and saline nasal douches alleviate the acute symptoms somewhat.

Perennial Hay-fever.—Since the cause and treatment of perennial hay-fever so closely duplicate those of bronchial asthma, perennial hay-fever should be treated as outlined in the chapter on Bronchial Asthma. Cutaneous tests will usually determine the causative protein which may be a food, pollen, animal emanation or dust, and omission of the protein usually brings relief. Animal emanation cases may be treated as described in the chapter on Bronchial Asthma and pollen cases may be treated as outlined for seasonal hay-fever. The inhalation of plant pollens at a definite season may predispose to a perennial hay-fever and a typical seasonal hay-fever caused by pollens may become a perennial hay-fever due to other superimposed causes; therefore pollen treatment should be given to those cases of perennial hay-fever that give positive pollen cutaneous tests. Cases of perennial hay-fever that fail to give positive cutaneous tests should be treated with autogenous vaccine made from the nasal secretion in the same manner as described under Vaccine Treatment of Bronchial Asthma. If stock vaccines must be used, a mixture of Streptococcus and Staphylococcus aureus seems to give the best results.

Pseudo-Hay-fever.—The treatment of pseudo-hay-fever depends chiefly upon the elimination or omission of the causative agents which may be classified as mechanical, chemical, odorific and thermal. Among the mechanical causes any kind of dust is the most frequent cause, more especially sweeping dust and hay dust; fine powder, such as talcum and the like, is also a frequent cause. Among the chemical irritants, soap powder, lye and ammoniacal fumes are very frequent causes. Among the odorific irritants, heavily scented perfumes, face powders, musty air and stable odors are frequent causes. Thermal irritants concern sudden changes of temperature, as in going from warm air to extreme cold, from moist air to very dry air, and exposure to drafts; a very frequent history is that of a paroxysm of sneezing with or without running of the nose on retiring and on arising. The mechanism of the latter seems to be a reflex due to the sudden exposure of the warm and protected skin of the body to cold air, as in getting out of bed and in undressing, during which acts the warm body surface is suddenly and momentarily exposed to cool air; in other words, there is a mild chilling of the body surface. The same mechanism holds for many who take cold easily. Occasionally pseudo-hay-fever patients are sensitive to some type of protein which may have rendered their nasal mucous membranes sensitive to those irritants. Appropriate protein treatment for those who are sensitive usually relieves

these symptoms, no matter what the irritant may be, and occasionally autogenous nasal vaccines will benefit or relieve the non-sensitive individual.

Vasomotor Rhinitis.—The treatment of this condition concerns the specialist in nose and throat diseases and he should be consulted first. Occasionally, however, cutaneous tests with proteins as used in perennial hay-fever and asthma will determine the cause. When the nose and throat specialist fails to relieve the symptoms and more especially in chronic infected sinuses, autogenous vaccines made from the nasal secretion or from the pus of the draining sinus, as already described in the chapter on Bronchial Asthma, frequently relieve and are desirable after treatment.

REFERENCES

Hall, H. M. Hay Fever Plants of California, Pub. Health Rep., Reprint No. 739, 803, April 7, 1922.

Watson, S. H., and Kibler, C. S. Etiology of Hay Fever in Arizona and the Southwest, Journ. Am. Med. Ass., lxxviii, 719, 1922.

CHAPTER II

BRONCHIAL ASTHMA

I. Chandler Walker

Since, at the present time, our conception of bronchial asthma differs radically from that of the past, it is desirable to describe briefly the modern clinical aspects of this condition in order that the treatment may be clearly understood.

TYPES OF ASTHMA

Typical Bronchial Asthma.—An attack or paroxysm of typical or true bronchial asthma consists of the following cycle of events. Some type of foreign protein, acting either centrally or peripherally as an irritant on the nerves that innervate the smooth muscular tissue lining the bronchi, causes a spasm or constriction of the bronchial musculature. The muscles of inspiration are equal to the task of drawing air through the constricted bronchi into the air cells of the lungs, but the elasticity of the lungs, together with the muscles of expiration, are not sufficient to expel the inspired air in the normal time, so that expiration becomes prolonged and is finally interrupted by an inspiration before the normal amount of air has left the lungs. Consequently, as the attack progresses, the lungs become overdistended with residual air, and sooner or later this overfilling of the lungs with air causes labored inspiration, although expiration remains more prolonged and more difficult than inspiration. The attack is now at its maximum and it may continue for only a few minutes or for a few hours. During the attack the patient develops a dry cough which, in a short time, may become productive in raising a more or less characteristic type of sputum. This sputum is thin, clear, slightly tenacious, and in it are suspended small white tapiocalike masses of mucus called Laennec's pearls. Microscopically eosinophils, Charcot-Leyden crystals, Curschmann's spirals, and small bronchial casts may be found; however, none of these elements are of clinical importance. The attack of asthma begins to subside when sputum is raised. A normal or subnormal tem-

perature and only a slight elevation of the pulse rate accompanies the attack. After the attack has subsided, the patient may be more or less fatigued but is otherwise normal and free from all symptoms until another attack is suddenly precipitated hours, days, or months later, depending upon when some foreign protein is again encountered.

On physical examination, during an attack of typical or true bronchial asthma, inspection verifies what has been already described, and in addition there may be some cyanosis. Percussion of the lungs during the height of the attack reveals a high-pitched resonance. On auscultation expiration is prolonged and feeble and inspiration is wheezing and accompanied by dry râles; after expectoration has developed there may be moist râles. Fluoroscopy of the chest at the height of the attack reveals a motionless diaphragm which seems to be fixed in a depressed position, and the lungs expand very slightly on inspiration.

Pathology has not advanced our knowledge of this condition, but by animal experimentation, however, the mechanism of a typical attack of true bronchial asthma is explained in the following manner: protein applied in the upper respiratory tract of an animal that has been rendered susceptible to or sensitized to that protein (Sewall) irritates the constrictor fibers of the vagus (Brodie and Dixon), producing a stenosis of the small bronchi by causing a spasm of their circular muscles (Auer and Lewis).

Atypical Bronchial Asthma or Asthmatic Bronchitis.—This atypical attack of bronchial asthma is usually associated with respiratory infections such as colds and bronchitis, chronic bronchitis, catarrhal conditions of the nose and throat, and occasionally with infections of the teeth, tonsils, and sinuses, and rarely with infections located in any part of the body. The primary cause is bacterial infection rather than protein sensitization. Patients with this type of asthma usually develop their attacks in one of two usual ways. The most common manner is as follows: The patient has been subject to bronchitis for a period of months or even years. During this time the symptoms of bronchitis have progressed and have become more and more severe. At first possibly there may be only a slight unproductive cough which may have followed a neglected cold; later the cough is more annoying and may become productive of expectoration. There may or may not be slight fever and the patient, since physical signs are practically negative, may be suspected of having tuberculosis. After a time there is some difficulty in breathing, especially on exertion. Later still respiration becomes wheezy and dry rhonchi are heard on auscultation. If these symptoms progress no further the condition is called bronchitis. If, however, the patient develops attacks of dyspnea (it is inspiratory in type) and suffocation, with or without exertion, the condition is called bronchial asthma. In reality the condition is a severe type of bronchitis and does not closely simulate typical bronchial asthma; the condition is more correctly asthmatic bronchitis.

The manner next most common to the foregoing in which patients develop this kind of asthma is as follows: As in the foregoing case, the patient becomes subject to chronic bronchitis and, although he is more or less troubled with it during the time he is awake, he is usually free from attacks of marked dyspnea and suffocation; but during his sleep the attacks appear and usually awake him in the early morning hours; this type of asthma most usually develops during or past middle age.

The sequence of events which takes place in these two types of attacks of atypical bronchial asthma or asthmatic bronchitis is as follows: The bacterial infection in the bronchi causes the usual type of bronchitic sputum which may be thick, but it is not very tenacious or jellylike, and it is raised with little difficulty ordinarily when the patient is not sleeping. At times, however, the sputum becomes very tenacious and jellylike and it clings so tenaciously to the lumen of the bronchi that repeated coughs may fail to remove it. The stimulus to coughing, however, is so great that the patient repeatedly coughs, and the more he coughs the more dyspneic he becomes until finally the tenacious secretion is raised, after which the patient rapidly becomes free from dyspnea. There is probably a slight constriction of the bronchial muscles, since the inhalation of fumes from antispasmodic remedies is followed by the raising of sputum and consequent relief from dyspnea. These drugs release the muscular constriction, thus leaving the secretion unattached. This muscular constriction, however, is not as marked as it is in the typical bronchial asthma as first described, neither is it caused by protein irritation of the nerves supplying these bronchial muscles. This slight muscular constriction in the atypical cases probably results from local irritation due to the protracted spell of coughing or less likely it is due directly to the irritation of the tenacious sputum. The dyspnea in these attacks is chiefly inspiratory in type and is due partly to the unproductive cough, and partly to the narrowed lumen of the bronchi; this narrowed lumen is due partly to slight muscular constriction and partly to the coating of tenacious mucus superimposed upon the constricted mucous membrane of the bronchi. After the acute attack has subsided, the patient is not entirely free from symptoms; he still has more or less cough and expectoration until another attack occurs; this may be a few hours later or not until the early morning hours of the next night. The duration of the attack may be a few minutes but more commonly it lasts an hour or two, and frequently the patient may continue in a more or less acute attack for several days. These attacks are frequently accompanied by a little fever and a slightly elevated pulse rate.

Physical examination of patients afflicted with this atypical type of bronchial asthma reveals, during the interval between attacks, signs of chronic bronchitis and emphysema. During the attacks the dyspnea is chiefly *inspiratory* in type, although both inspiration and expiration are prolonged, but the patient manifests the greater effort on inspiration, and

in addition to the wheezing and dry rhonchi there may be heard coarse bubbling râles in the bronchi. The patient himself describes the dry râles as whistling and the wet râles as rattles. Fluoroscopy of the chest during the attack reveals a diaphragm fixed in about the normal position, midway in its greatest excursion, thus indicating no great amount of distention of the lungs. The lung vital capacity is low in these cases between the attacks at a time when the patient is most free from symptoms; this indicates a state of permanent emphysema. Pathology and X-ray reveal a peribronchial thickening.

All cases of bronchial asthma cannot be placed at first in either of the two groups as already described, namely, typical and atypical; however, the history, which may be elicited from the patient, describing the onset and the first attacks will aid greatly in determining the kind of asthma and the cutaneous or skin test will definitely determine this, so that after the case has been completely investigated there is no difficulty in determining the type of asthma.

Obsolete Types of Asthma.—It is necessary to discuss briefly other types of asthma which should not be interpreted as or mistaken for bronchial asthma. Cardiac asthma and renal asthma are symptoms of cardiac and renal disease rather than types of bronchial asthma; cardiac and renal dyspnea are better terms. The dyspnea of laryngeal and tracheal obstruction, the dyspnea caused by compression of the trachea or bronchus by mediastinal tumors, aneurysm, enlarged bronchial glands, enlarged thymus and the like should be distinguished from bronchial asthma. Hysterical dyspnea, a foreign body in a bronchus, localized foci of tuberculosis in the bronchial glands, chronic fibrinous bronchitis and emphysema per se should likewise be differentiated from bronchial asthma. Although bronchial asthma may complicate many of the above conditions, the asthmatic element should be considered as entirely separate.

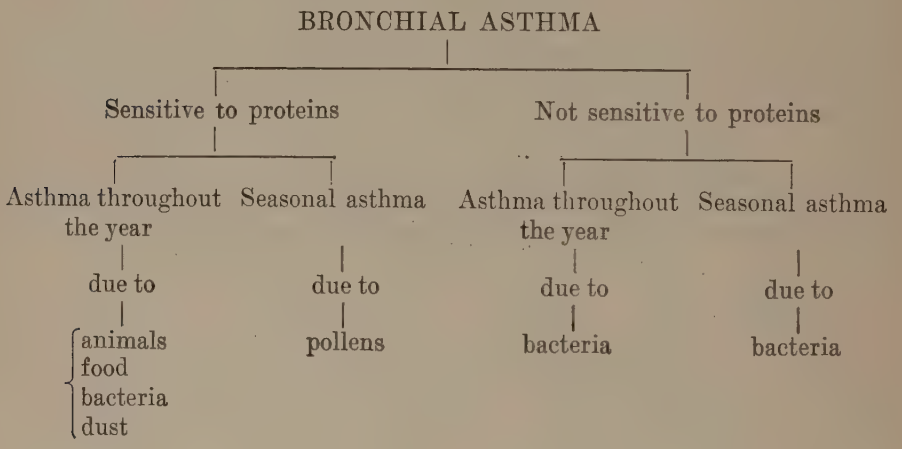
TREATMENT OF BRONCHIAL ASTHMA

Protein Sensitivity.—There are several methods of determining whether a patient is sensitive to a protein or not. One way which is used more or less is the intradermal or intracutaneous injection of the protein; there are, however, some objections to this method and it tends to be too delicate if not non-specific. A test which is used more extensively and which is very reliable is the cutaneous or skin test, which is performed in the following manner: A number of small cuts, each about an eighth of an inch long, are made on the flexor surfaces of the forearm. These cuts are made with a sharp scalpel, but are not deep enough to draw blood, although they do penetrate the skin. On each cut is placed a protein and to it is added a drop of tenth normal sodium hydroxid

solution to dissolve the protein and to permit of its rapid absorption. At the end of a half hour the proteins are washed off and the reactions are noted, always comparing the inoculated cuts with normal controls on which no protein was placed. A positive reaction consists of a raised white elevation or urticarial wheal surrounding the cut. The smallest reaction that we call positive must measure 0.5 cm. in diameter. All larger reactions are noted by a series of plus marks and any smaller reaction is called doubtful. The cutaneous or skin test, therefore, not only separates true or typical bronchial asthma from the atypical or asthmatic bronchitis but also it determines the proper treatment.

Specific Protein Treatment.—This treatment depends entirely upon the cause and consequently it will be considered in conjunction with the above classification of causes; in other words the various types of proteins that cause bronchial asthma will be taken up in the same sequence as they appear in the above classification and the proper treatment will be discussed.

Classification of Causes of Bronchial Asthma.—By means of the cutaneous or skin test the causes of bronchial asthma may be classified in the following manner and proper treatment is thereby clearly determined.



Animal Emanations Causative of Asthma.—The inhalation of the proteins contained in the hair, dandruff, and skin dust of the horse, dog, cat, of fur-bearing animals such as pets and fur-wearing apparel, and the protein in the feathers of chicken and goose are frequent causes of asthma. When these are the cause of asthma, it is best and usually satisfactory to dispense with the source of the protein; that is, discard the feather pillows, get rid of the cat, dog, rabbit or parrot and discontinue the wearing of the fur neckpiece or coat as the case may be. Very often, when horses are the cause, the patient is too sensitive to the protein to be able

to avoid it. For instance there may be sufficient horse dust in the streets, or he may live near a stable; furthermore he may wish to be near or to drive horses. In such instances the patient may be treated in the following manner: do cutaneous tests with different dilutions of the protein and begin subcutaneous treatment with the strongest amount that fails to give any reaction whatsoever. As an example, the patient gives a positive test with a 1:1,000 dilution, a doubtful reaction with a 1:10,000 dilution and a negative reaction with a 1:100,000 dilution. With such a case begin treatment with the 1:100,000 dilution giving subcutaneously 2 or 3 minims or 0.1 c.c. of the 1:100,000 and once each week increase the dose 1 minim or 0.05 c.c. until 11 minims or 0.7 c.c. is given at one time. After this the next strongest dilution, namely 1:10,000, may be given in the same scale of doses and so on through the 1:1,000 dilution and a 1:200 dilution. Usually the patient is completely desensitized and practically always free from symptoms when this schedule is finished and frequently symptoms from horse exposure disappear early in the course of treatment. Naturally should the patient's surroundings or desires make it advisable to treat for any of the other animal exposures, the same method would prevail for that particular animal emanation protein.

Food Proteins Causative of Asthma.—Food proteins often cause asthma through inhalation of the flour of the cereal grains. Such instances are confined to bakers, housewives, cooks, grain merchants and store keepers, all of whom handle the various types of flour and ground-up grain. The best and most satisfactory way of treating these cases is to have the patient avoid the flour dust, even though a change of occupation is necessary.

The most usual manner in which patients have asthma from foods is by the ingestion or eating of them. Cereal grain flour (chiefly wheat), eggs and milk are the most common foods to cause asthma. In the case of wheat flour, the patient may eat shredded wheat biscuit, puffed wheat and thoroughly toasted bread, because the exposure of the flour protein to extremely high temperatures destroys the anaphylactic or poisonous element. Other foods containing white flour should be omitted from the diet and it is often necessary to remind the patient that macaroni, spaghetti, thickened gravies, dark breads, crackers and the like contain white flour and consequently should be avoided. In testing with milk, it is essential to use two proteins, namely, casein and lactalbumin because when only the lactalbumin reacts positively the milk may be heated until the lactalbumin coagulates in the form of a scum on the surface of the milk and this coagulated lactalbumin or scum may be removed and the remaining milk may be taken. When casein reacts positively, milk should be avoided. In the case of eggs, the white and the yolk may be tested separately since occasionally only one part of the egg may be positive and

the part failing to react may be eaten. The patient may eat baked potato when boiled potatoes cause trouble.

Although any food protein may cause asthma, it is the food that is frequently or constantly eaten that causes asthma for which the patient seeks relief, because the patient is able to determine the offending food occasionally eaten and the attack of asthma which soon follows impresses the fact upon the patient that every time he eats that particular food he has asthma. Therefore in addition to what has been already mentioned each patient should be tested with the foods that he is accustomed to eat frequently, namely, the cereals, the meats, the common vegetables, common fruits and fish, and treatment should consist of avoiding the foods that cause a cutaneous reaction. Occasionally a patient may eat small amounts of the offending protein, whereas larger amounts cause symptoms.

Nursing infants should be tested with a similar list of food proteins since it is now known that sufficient food protein may be present in mother's milk to cause asthma in the nursing infant (O'Keefe, Shannon).

Although absolute omission of the offending food protein is entirely satisfactory and not nearly as difficult as might be anticipated, there are methods of treating or desensitizing for foods. As already outlined for horse asthma, the food case may be tested and treated with subcutaneous inoculations of various dilutions of the offending food protein, but the process is a long and tedious one and this method is less satisfactory than the following method of feeding protein. Schofield was probably the first to overcome sensitization with food proteins by feeding them. He gave his patients pills containing minute amounts of the offending protein, gradually increasing the dose until large amounts were taken without symptoms. Although it required two years before the patient was able to eat a whole egg, the cure seems to have been permanent. Rich, in the same manner, accomplished similar favorable results in a year's time. The difference in the length of time depends upon the size of the initial amount which the patient can take without symptoms. Schloss and Talbot have had success with this kind of treatment, and Grover has had some success by feeding the food protein in a liquid form. All of these writers were dealing with young children whose parents were sufficiently conscientious to make a go of it. The author has tried this treatment with adults, but none has been conscientious enough to take the proteins per schedule for any length of time.

Bacterial Proteins Causative of Asthma.—As a rule, bacterial proteins do not cause asthma, and cutaneous tests with these are of little avail. In case bacterial proteins are desired for testing, it is the protein of Streptococcus hemolysans and viridans, Staphylococcus aureus and albus and pneumococcus Type IV that should be employed. Treatment should consist of giving a vaccine of the organism that caused a reaction. It should not be misunderstood that bacteria do not cause asthma, because

they very often do cause it; however, it is their infectious element rather than the protein element that causes symptoms. This bacterial cause of asthma will be discussed later on under Vaccine Treatment.

Organic Dust Causative of Asthma.—The inhalation of dust from the cereal grains has already been discussed under Foods. Room dust and street dust may cause asthma because of the presence of animal emanations; the rôle of dust has already been sufficiently described under Animals Causative of Asthma. Face powders containing orris root and rice sometimes cause asthma and these may be detected by doing cutaneous tests with orris root and rice protein; treatment consists of elimination. Sifters of green coffee beans, jewel polishers and fur dyers have been known to become sensitive to the dust of their occupations. Positive cutaneous tests have been obtained with these substances, namely, raw coffee in the case of coffee sifters, boxwood and orange wood in the case of jewel polishers, and fur protein and dyes in the case of fur dyers. If avoidance of these dusts is impossible, treatment with subcutaneous inoculations, depending upon tests with various dilutions of these proteins (as outlined under Animals Causative of Asthma), is curative. These and other organic dusts cause asthma because of sensitization of the patient to them and this condition should not be confounded with the fact that inorganic dust which does not sensitize often causes asthma because of mechanical irritation. Examples of inorganic dust irritation are chalk dust and ordinary dirt, which is a part of house and street dust; these naturally do not cause sensitization.

Pollens Causative of Asthma.—Since the seasons of pollination of the plants vary in different localities, it is essential to learn the seasons of pollination in the patient's locality in order to know with what pollens the patient should be tested and treated. In the East and Middle West we recognize three distinct seasons, namely: February to June during which time the trees pollinate; May to August during which time a great many plants pollinate; and August to October during which time the compositæ pollinate. In the South and West each of these seasons is earlier and usually there are two seasons of pollination of the grasses, one very early in the spring and the other later in the summer. As a rule, tree pollens rarely cause asthma. Of the early summer pollens, the grasses are the chief cause of asthma, and of the late summer pollens, ragweed is the chief cause. For a detailed description of the causative pollens and pollen treatment of asthma, reference may be made to the chapter on Hay-fever in order to avoid unnecessary duplication. The cause and treatment of pollen asthma do not differ from those of hay-fever.

Vaccine Treatment of Bronchial Asthma.—Treatment with vaccines concerns chiefly the non-sensitive type of bronchial asthma, namely, the asthmatic bronchitis type which fails to give positive protein tests and which usually is caused by bacterial infection. The bacterial infection is

chiefly present in the bronchial tubes, in which case the patient's thick sputum contains the causative bacteria. Occasionally when the patient has little chest sputum, a catarrhal secretion of the nose or throat, or an infected sinus harbors the causative bacteria and rarely infected teeth are the source of the bacteria. The causative organisms are usually the streptococcus group, although Staphylococcus aureus, diphtheroids and pneumococci sometimes cause asthma. Rarely other respiratory tract organisms may be the cause.

If stock vaccines must be used, those containing chiefly streptococci are the choice; however, in each case the use of a stock vaccine is merely a guess at the causative bacteria. Autogenous vaccines are by far the best since they offer the best chance of obtaining the causative bacteria. In making autogenous vaccines, thick masses of sputum, which are raised at the end of an attack or come from the smaller bronchi, are washed in sterile saline, shaken in bouillon, and plated on blood agar. From the blood agar plates the predominating organism may be selected. Equally good results follow from inoculating and growing the washed sputum in dextrose bouillon, and from this the vaccine is made. In a similar manner vaccines may be made from nasal secretion, or from the pus from an infected sinus or tooth.

Vaccine treatment should be given preferably at weekly intervals and never oftener than at five-day intervals. The first dose of vaccine for adults should approximate 200,000,000 or 300,000,000 and each succeeding dose should be increased 100,000,000 until at least 1,000,000,000 is given at one time. If the patient is improving under such treatment it is best to continue increasing the dose up to 2,000,000,000 or until relief is obtained; if no benefit has resulted it may be best to make a new vaccine. Any dose that causes much local or any systemic reaction should be repeated once before the next increase of dosage is given.

With the non-sensitive cases, the older the patient is when asthma begins and the older he is when vaccine treatment is begun, the more unfavorable the prognosis; age to a certain extent is an index to individual resistance. The permanency of relief from vaccine treatment in the non-sensitive cases depends on the individual's resistance to the bacteria in question; therefore, the duration of relief from asthma varies. Some patients continue free from asthma for many months after vaccines are discontinued, others for only a month or two, and some patients require the constant use of vaccines to be free from asthma. Succeeding courses of vaccine treatment, provided that there has been no change in the bacteria which are causing the relapse, seem to relieve more promptly than the first course of vaccine treatment. When a relapse is not relieved by a second course of vaccines which previously did relieve, other bacteria should be suspected as the cause of asthma and new vaccines should be made.

Frequently the sensitive patient whose asthma is primarily caused by animal emanations, food, pollens or dust may need autogenous vaccine treatment in addition to the specific protein treatment. Vaccine treatment in these patients may be necessary in order to benefit an accompanying or a resultant bronchitis; furthermore the condition of frequent colds, which often are associated with true bronchial asthma and which do precipitate attacks, is benefited by vaccine treatment.

Non-specific Protein Treatment.—As in most chronic infections intravenous foreign protein treatment may be of benefit, the same may apply to the asthmatic patient. Auld reports good results from the intravenous injection of peptone; before trying this, however, the patient should be tested with peptone to be sure he is not sensitive. In a similar manner typhoid vaccine has been used intravenously. Giving peptone in capsules by mouth an hour before each meal has yielded favorable results in the hands of Vallery-Radot and others. The author has had little success with these methods and since non-specific treatment does not throw any light on the actual cause of the disease it seems best to use specific treatment when possible and autogenous vaccines when specific treatment fails or cannot be given.

Tuberculin Treatment of Bronchial Asthma.—Patients who have both tuberculosis and bronchial asthma or, probably more correctly, asthmatics who give a positive von Pirquet test, have been greatly benefited or relieved of asthma by tuberculin treatment (Van Leeuwen, Pietroforte). Van Leeuwen gives dilutions of Koch's T. O. A. subcutaneously, beginning with 1 c.c. of a 1: 100,000 dilution and increasing the dose slowly at irregular intervals. The author has not had an opportunity to try out this treatment so far, since the combination of asthma and pulmonary tuberculosis is rare in his experience; however, tuberculin treatment in the non-tuberculous asthmatic has been thoroughly tried by the author and failed.

Operative Measures.—Although bronchoscopy and intratracheal treatment is not essentially an operative procedure, it is sufficiently removed from the clinician's armamentarium to warrant the consideration of it along with operative procedures. De Levie anesthetizes the bronchi by spraying them through a bronchoscopic tube with novocain and epinephrin. Cases having much secretion from bronchitis were not benefited because, as he thought, the secretion prevented the spray from reaching the mucous membrane of the bronchi.[1]

Climate.—Change of climate does not benefit the sensitive type of patient, with the exception of the pollen cases, with whom the change is in reality from a place where those particular pollens are prevalent to a place where they are absent. In a similar way a patient may move from close

[1] It is hardly necessary to state that nasal operations for establishing free drainage of infected sinuses or for the removal of nasal polypi are indicated.—Editor.

proximity to a stable to a place more distant. With the non-sensitive or asthmatic bronchitis type of case a change of climate occasionally benefits or relieves attacks; even moving for a short distance, as from low ground to high ground, and vice versa, may relieve; but such instances are not common. Florida is a suitable place for an occasional case, Arizona for still another, California for a third, and so on, but no one of these states or climates is suitable for all three; it is an expensive experiment and usually a bad investment.

Supportive Treatment.—Rarely one meets with sensitive cases and frequently one meets with non-sensitive cases who do not improve under what is probably the proper treatment according to experience. It is these patients who require supportive treatment, such as tonics, rest, proper diet, restricted exercise, fresh air, and hygienic measures. In such cases it is necessary to remove the burdens and handicaps before the patient is able to respond to proper specific treatment.

Drug Treatment.—The drug treatment of bronchial asthma is most disappointing. In the asthmatic bronchitis type potassium iodid in 0.6-gm. (10-gr.) doses three times a day is of considerable service. This drug thins the secretion in the bronchi, thus enabling the discharge of an otherwise thick, tenacious sputum, which, when not easily raised, causes choking up, severe coughing spells, and asthmatic attacks. In other words, potassium iodid favors free drainage from the bronchi with slight effort: a bronchial cathartic. This drug, however, does not benefit the sensitive type of asthma, which is not complicated by severe bronchitis. The incorporation of small amounts of codein with the potassium iodid is serviceable in allaying undue irritation. Benzyl benzoate by mouth sometimes seems to benefit children, but it is of little value in adults. Intravenous treatment with sodium iodid in 1-gm. doses sometimes benefits; atropin subcutaneously in large doses and aspirin by mouth occasionally give temporary relief. The most reliable and yet the most harmless drug that temporarily relieves the acute attacks of either type of asthma is epinephrin. This is obtained as adrenalin chlorid 1:1,000 (Parke, Davis & Co.) and should be administered subcutaneously in ½-c.c. doses for adults, repeated as often as necessary. This drug should not be given intravenously or intramuscularly, and large doses should be avoided in children, with whom 0.2 to 0.3 c.c. suffices as a rule. Since the patient himself cannot use hypodermic medication, he tends to rely upon patent medicines and so-called asthma cures. The most serviceable among these seem to be the ones that contain stramonium leaves and saltpeter in the form of a powder, the fumes of which when burned are inhaled for the relief of the paroxysm. These fumes seem to be antispasmodic in action and following their inhalation thick sputum is raised and temporary relief results. Many other drugs might be mentioned, but they are less reliable.

REFERENCES

Auer, J., and Lewis, P. A. Journ. Exper. Med., xii, 151, 1910.
Auld, A. G. Brit. Med. Journ., ii, 49, 1918.
Brodie, T. G., and Dixon, W. E. Journ. Physiol., xxix, 97, 1903.
De Levie, D. J. Nederl. Tijdschr. v. Geneesk., i, 221, 1918.
Grover, J. I. Personal Communication.
Levie, de, D. J. Nederl. Tijdschr. v. Geneesk., i, 221, 1918.
O'Keefe, E. S. Journ. Am. Med. Ass., lxxviii, 483, 1922.
Pietroforte (Maragliano, P.). Riforma med., No. 29, xxxvi, 641, 1920.
Rich, H. M. Journ. Mich. State Med. Soc., xiii, 649, 1914.
Schloss, O. M. Am. Journ. Dis. Child., iii, 341, 1912.
Schofield, A. T. Lancet, i, 716, 1908.
Sewall, H. Journ. Lab. & Clin. Med., ii, 874, 1917.
Shannon, W. R. Am. Journ. Dis. Child., xxii, 223, 1921.
Talbot, F. B. Boston Med. & Surg. Journ., clxxv, 191, 1916.
Vallery-Radot, Pasteur. Ann. de méd., iv, 503, 1920.
Van Leeuwen, W. S. Lancet, ii, 1366, 1921.

CHAPTER III

SERUM DISEASE AND SERUM ACCIDENTS

GEORGE M. MACKENZIE

With the increase in recent years of various forms of serum therapy, the clinical problems of serum disease and serum accidents have become correspondingly more important. The serum from actively immunized animals is now almost universally used in diphtheria, tetanus and Meningococcus meningitis; in lobar pneumonia (Type I) and dysentery, immune serums are extensively used and in other infectious diseases efforts are made from time to time to develop therapeutic serums. In the preparation of these serums horses have been almost exclusively employed and therefore the foreign serum which produces the symptoms of serum disease is in the great majority of instances horse serum. In this discussion of the phenomena dependent upon the parenteral administration of a foreign serum, we are not concerned with the specific antitoxic, opsonic, lytic or agglutinating properties of the serum, but simply with the results of administering to a patient, intravenously, subcutaneously, intramuscularly or subdurally, the serum from an animal of an alien species.

From the clinical point of view, particularly, it is well to keep in mind the distinction between *serum disease* and *serum accidents*. The term serum disease is used for the group of symptoms which occurs in an individual who is not hypersensitive to the foreign serum administered, while serum accident is reserved for the sudden, often alarming or even fatal, reaction which occurs in an individual who is hypersensitive to the kind of serum administered. For practical purposes this division amounts merely to a distinction drawn between the reaction to horse serum by nonsensitive and hypersensitive individuals. Serum disease may be looked upon as the natural, and, if sufficiently large quantities are given, nearly constant, response to a foreign serum by an individual with normal reactivity to the serum employed. Serum accidents are the untoward effects of giving serum to an individual who has a specific hypersensitiveness to that kind of serum.

SERUM DISEASE

Incidence.—Not every patient receiving a parenteral injection of serum develops serum disease, even though quantities up to 1,000 c.c. or more be injected in the course of a few days. It is clear, therefore, that individual susceptibility is one of the factors which determine the incidence of serum disease. As we shall see in a later paragraph, observations on this group of patients who are naturally insusceptible to serum disease have perhaps given a clew to an understanding of certain phases of the underlying mechanism in serum disease. In addition to differences in susceptibility among individuals of the same race, there is evidence that certain races are less susceptible than others. The North American Indians are less susceptible than the white race, and in negroes there seems also to be a relatively low susceptibility. For some quite obscure reason the serum from different horses does not always exhibit a uniform capacity to produce serum disease. Numerically the foregoing factors affecting the incidence of serum disease are of much less importance than the amount of serum administered. The published figures on the frequency of serum disease vary over a wide range, largely because of differences in the quantity of serum used. When such small amounts as are commonly

Frequency of Serum Reactions With Different Quantities of Serum *

Total Amount of Serum	Cases Showing Reaction	Cases Observed 10 Days or More Showing No Reaction	Total Cases	Per Cent of Cases Showing Reaction
1- 9 c.c.	9	73	82	10.9
10- 19 c.c.	52	137	189	27.5
20- 29 c.c.	40	100	140	28.5
30- 39 c.c.	28	47	75	37.3
40- 49 c.c.	19	26	45	42.2
50- 59 c.c.	15	16	31	48.3
60- 69 c.c.	17	23	40	42.5
70- 79 c.c.	14	7	21	66.6
80- 89 c.c.	8	12	20	40.0
90- 99 c.c.	7	2	9	77.7
100-109 c.c.	4	5	9	44.4
110-119 c.c.	3	1	4	75.0
120-129 c.c.	1	1	2	50.0
130-139 c.c.	4	2	6	66.6
140-149 c.c.	3	1	4	75.0
150-159 c.c.	2	1	3	66.6
160-169 c.c.	2	2	4	50.0
170-280 c.c.	8	0	8	100.0
Total	236	456	692	34.1

* Weaver.

used in diphtheria immunization and treatment are employed, a large percentage of the patients have no obvious manifestations of serum disease; but when, as in the use of antipneumococcus Type I serum, amounts from 100 c.c. to 1,000 c.c. or more are injected, a very small percentage of patients escapes at least some distinct evidence of serum disease. In a recently tabulated series of 100 consecutive patients with lobar pneumonia treated with serum at the Presbyterian Hospital, New York, 93 per cent developed symptoms of serum disease. Weaver's report furnishes the most satisfactory evidence on the relation of the amount of serum to the incidence of serum disease.

Whether other factors, such as the age of the patient, the disease for which the serum is given, or the route of administration,[1] affect the incidence of serum disease is uncertain; but any effect which they may have must be of relatively small numerical importance.

Incubation Period.—In patients who have had no previous serum treatment and who are not spontaneously hypersensitive to horse serum, the interval between the first injection of serum and the appearance of the first symptoms of serum disease is, in a large majority of cases, between six and twelve days. In a small percentage of patients the incubation period may be two weeks or longer, and there are cases on record in which the incubation lasted more than three weeks. Of considerable interest are cases with short incubation periods. We have a number of times observed patients, presumably receiving serum for the first time, who developed typical serum disease on the third or fourth day. With such patients there is frequently an uncertainty as to whether they have forgotten a previous serum injection, as might readily occur after an immunizing dose of diphtheria antitoxin in childhood. Some of these patients also may have a spontaneous hypersensitiveness to horse serum of such low degree that there is nothing either in skin tests or history to indicate the fact. We are not referring here to the not uncommon immediate and transitory reactions which occur in patients receiving serum for the first time. It is a fairly common experience in giving large doses of serum intravenously to observe, either while the serum is being given or within two hours, such symptoms as chill, rise of temperature, cough, cyanosis and perhaps a transitory urticarial or erythematous eruption. Such reactions usually subside within an hour or two but, if alarming, may be relieved by a subcutaneous injection of epinephrin, 0.5 to 1.0 c.c. It seems probable that they represent a foreign protein reaction quite analogous to what occurs after the intravenous injection of killed typhoid bacilli or sterile milk. Except for the occasional occurrence of an eruption during these reactions, their symptomatology is not that of serum disease. In the pioneer studies of serum disease by von Pirquet and Schick, attention was called to the fact

[1] Rolleston has not found after intrathecal administration a higher incidence than is observed after subcutaneous injection.

that patients who receive a reinjection of serum about two weeks or more after the first serum treatment manifest a shortening of the incubation period. They described an "immediate reaction" occurring within the first twenty-four hours and characterized by fever, eruption, swelling of face and particularly the lips, and short duration. This type of reaction has no sharp line of demarcation from what we shall describe as serum accidents. Von Pirquet and Schick believed that the "immediate reaction" was most likely to occur if the reinjection was made during the period from twelve days to five months after the first injection. They also described an "accelerated reaction" which might be expected if the reinjection was given three weeks or more after the first injection. The symptoms of the accelerated reaction are similar to those of the usual form of serum disease but the incubation period is two or three days shorter. There is a period, therefore, according to von Pirquet and Schick, during which both immediate and accelerated reactions may be expected. The principle of shortened incubation period following reinjection has been abundantly confirmed, but the idea that the occurrence of an "immediate," an "accelerated" or both types of reaction may be predicted from the amount of time elapsing between primary and secondary serum injections has not been substantiated.

Symptomatology

There is a wide range of variation in both the intensity and the duration of symptoms. Even after the administration of 1,000 c.c. or more of serum the only symptoms of serum disease may be a mild pruritus and a scattering crop of urticarial wheals or erythematous blotches with or without slight enlargement of the superficial lymph-nodes. The symptoms in such mild cases may be present for only a single day, and may easily be missed if one is not on the lookout for them. From these cases with inconspicuous symptoms there are all gradations in severity up to cases like the following which illustrates the severe form occasionally encountered.

M. M., single woman of 23, admitted to the hospital April 9, 1919, on the third day of her illness. Lobar pneumonia twice previously, but no serum therapy of any kind before admission. No history of asthma, hayfever, eczema or hives. Physical examination showed frank consolidation of both lower lobes. Blood culture sterile. Pneumococcus Type I recovered from sputum. Blood count: W.B.C. 32,000; polymorphonuclears 94 per cent. Temperature 103.4° F., pulse 114, respiration 40. Intracutaneous test with 0.02 c.c. horse serum 1 : 10 negative. During the second and third days in the hospital patient was given by intravenous injections 400 c.c. of antipneumococcus Type I serum. Temperature fell by lysis and reached normal on the ninth day of her illness—5 days after the first serum treatment. Two days later enlarged lymph-nodes which later be-

came tender were noted in each axilla, and urticaria with erythema and marked pruritus appeared on face, arms, legs, and back. The eruption soon spread over the entire body; all the superficial lymph-nodes became moderately enlarged. On the fifth day of the serum disease the eyelids, face and forehead became edematous. The next day temperature rose to 103.8° F. and patient complained of pain in the back of the neck and in scapular regions. The next day shoulders were painful but there was no objective evidence of arthritis; elbows became painful and red. The erythematous and urticarial eruption with pruritus was present continuously for 13 days; there was fever for 15 days, the highest temperature recorded being 104.8° F. on the sixth day of the serum disease and the second day after the onset of fever. Arthritis was present 8 days and was not relieved by aspirin gr. xl per day. The spleen was not felt. Blood count at the height of the serum disease was W.B.C. 6,400, polymorphonuclears 56 per cent, large mononuclears 15 per cent, transitional 5 per cent, lymphocytes 14 per cent, eosinophils 8 per cent, basophils 2 per cent. The duration of the serum disease from the appearance of the eruption to the return of temperature to normal was 21 days. So far as the pneumonia was concerned the patient made an uncomplicated recovery; there was no evidence that anything but the serum disease was responsible for the temperature.

Cases of serum disease like the above are uncommon; the possibility of their occasional occurrence should not deter one from giving a serum of therapeutic value. Serum disease itself is probably never fatal. So far as the writer is aware there is no record of a fatality occurring in a non-allergic individual receiving serum for the first time, in which death could be attributed to the serum disease. Most cases have a few days of discomfort from pruritus or arthritis but rarely any severe distress. The various symptoms will be considered in order.

Eruption.—The most common symptom of serum disease is a cutaneous eruption and the most common form of eruption is an urticaria or a combination of urticaria and erythema. The appearance of wheals or a patchy erythema is frequently preceded by itching of the skin. The visible eruption is apt to begin with a few scattered wheals on the face or extremities. They increase in size and number and by the end of from twenty-four to thirty-six hours may involve the entire body. They may be large and confluent or small and discreet with or without areas of erythema irregularly interspersed. Some cases show only patchy or punctate erythema without wheals; in others the eruption may be morbilliform or multiform with a tendency to form circinate lesions. Exceptionally it may resemble the eruption of either measles or scarlet fever. A rare form of rash is that in which the eruption is dominantly purpuric; the three patients in whom this has been observed by the writer have all had serum disease of more than average severity. In patients to whom the serum has been administered subcutaneously the eruption may be confined to the

area around the site of injection—the so-called local serum disease; but more frequently in such cases it begins as a local eruption and later becomes generalized, sometimes with an interval of days between the local and generalized skin phenomena.

Lymph-nodes and Spleen.—Although the eruption is apt to be the first symptom noted by the patient, if one is looking carefully for the onset of serum disease a considerable percentage of cases will be found to have enlarged lymph-nodes for a day or two before the appearance of the rash. Frequently the epitrochlears are the first nodes palpably enlarged, and following them the cervical, axillary and inguinal groups develop several nodes from split-pea to hazelnut size. They are discrete, freely movable and often, but not always, tender. It will usually be found that the enlargement of the lymph-nodes persists for several days after all the other symptoms of serum disease have subsided. When the serum has been administered under the skin or into the muscles, the regional nodes are usually the first involved. A small percentage of cases show no palpable enlargement of any lymph-nodes throughout the course of the serum disease.

If sought for every day enlargement of the spleen may occasionally be demonstrated. We have never observed more than slight enlargement; the splenic edge is felt 1 to 3 cm. below the costal border; after two or three days it is no longer palpable.

Arthritis.—Reports by different observers give the frequency of joint symptoms as low as 20 per cent and as high as 60 per cent of all serum disease cases. At the Presbyterian Hospital the incidence has been close to the upper figures. There is in most cases a striking contrast between subjective and objective phenomena. The painful joints cause the patient more distress than any of the other symptoms and he may occasionally have almost as much pain as the rheumatic fever patient, but examination in most cases reveals little except tenderness and limitation of function by pain. Exceptionally (about 10 per cent) there are the signs as well as the symptoms of an acute arthritis with all the cardinal symptoms—swelling, redness, heat, tenderness and fluid in the joint cavity. When aspirated and examined, such fluid has been shown to possess the characteristics of the fluid of true arthritis. It is turbid; there is an increase in cells up to 22,000 per c.mm.; in the more severe cases the polymorphonuclear cells usually predominate, but even with high cell counts mononuclear cells may be more numerous; horse serum may be present in demonstrable quantities. The joints commonly involved are the knees, ankles, elbows, wrists, and small joints of hands and feet; less commonly the hips, vertebral and clavicular joints. In contrast with rheumatic fever a considerable percentage show involvement of the temporomaxillary joints. It is the rule for the joint symptoms to appear several days after the onset of the exanthem, sometimes, even, after the skin manifestations have entirely subsided. Rarely the arthritis appears before the exanthem.

Fever.—Approximately 30 per cent of patients with serum disease have fever. Often it is difficult to decide whether a temperature which is present during the serum eruption is due to the disease for which serum was administered, to a complication, or to serum disease. As with other symptoms the severity and duration of the temperature reaction show wide variations. From cases in which there is an elevation of only a degree for a day or two all gradations are observed up to those who have a temperature between 102° F. and 104° F. for from twelve to fourteen days. The pulse rate increases proportionately and tends to fluctuate parallel with the temperature.

Edema.—About one-third of all cases have obvious edema. If slight, it may be confined to the face and particularly to the loose tissues about the eyes. The pretibial regions, the ankles, the hands and arms are next in order of frequency of involvement. Less often the back, chest, genitals, and sacral region are perceptibly edematous. Roughly, therefore, the distribution is that of a nephritic edema; investigations have indeed shown that with, and also sometimes without, the appearance of edema a measurable renal insufficiency develops. There may be chlorid and water retention, a lowered phthalein excretion, diminished volume output, albuminuria and cylindruria, but rarely, if ever, a demonstrable nitrogen retention. The evidences of impaired renal function are transitory and leave behind nothing to suggest that the kidney has been permanently damaged. Such mild and evanescent manifestations of injury to the kidneys constitute in no sense a contra-indication to the use of an effective serum.

Optic Neuritis.—Recently it has been reported that optic neuritis occurs in some cases of serum disease. While we have insufficient data for a statement concerning its frequency, we can corroborate Mason's observation. In the reported cases there was, in addition to the edematous retina and hyperemic swollen disks, an increase of cells and globulin in the spinal fluid.

Blood.—Many cases of serum disease in adults show no alteration in the blood picture. Von Pirquet and Schick in their studies of serum disease in children found that during the incubation period there is a leukocytosis which, with the development of symptoms, is succeeded by a leukopenia caused by diminution of the polymorphonuclear cells. In adults we have not observed these blood changes with anything approaching regularity. Many cases, even at the height of severe symptoms, have shown no alteration of either the total or differential counts; a few have had a leukocytosis of from 12,000 to 15,000 and toward the end of or after serum disease an eosinophilia has been observed in a few cases; but we believe that noteworthy blood changes, especially the leukopenia, are less common in adults than von Pirquet and Schick found them in children.

Other Occasional Symptoms.—Abdominal pain, vomiting, diarrhea, stupor, headache, conjunctivitis, and sore-throat occur occasionally during serum disease without anything else to which they can be attributed. Not infrequently, also, patients are seen who, after a typical serum disease has subsided, continue to have an unexplained temperature for a week or more. Since, in such cases, the patients have just passed through an infectious disease, it is rarely possible to rule out with certainty some complication of the infectious disease as a cause of the temperature rather than the serum disease. However, the unconfirmed suspicion remains that sometimes fever of this kind may be due to the foreign serum. Godall has also mentioned this possibility. In his report on serum disease following intrathecal injections, Rolleston mentions the occurrence, in a small proportion of cases, of meningeal symptoms simulating a recurrence of the meningitis for which the serum was given.

Relapses.—Among the large number of nitrogenous substances which horse serum contains, there are at least three or four distinct proteins capable of independent antigenic action. With this in mind, and recalling the observation of Dale and Hartley that an animal sensitized to a foreign serum may show sensitization to the albumin later than to the globulin, the possibility that "relapses" in serum disease are to be explained by reactions to different antigens of the horse serum at different times suggests itself. Such an assumption is supported by the investigations of Coca who found that, with a diphtheria antitoxin consisting of the isolated pseudoglobulin, there were no instances of relapse in 129 cases of serum disease.

Any or all of the symptoms of serum disease may occur during the relapse and it may be either more or less severe than the primary reaction. The exanthem of the relapse is less likely to be predominantly urticarial; more often it is erythematous or morbilliform. The interval between the two periods of symptoms may be as much as two weeks but more commonly it is from four to seven days.

Differential Diagnosis

Rarely does serum disease present any difficulty in diagnosis. The exanthem, enlarged lymph-nodes, edema, arthritis and fever occurring after the administration of a foreign serum can hardly be confused with anything else. However, the occurrence of a relapse with an erythematous or morbilliform eruption may cause uncertainty. We have also seen a patient go through a typical serum disease and then a week later develop an arthritis of the temporomaxillary joints with fever and no eruption. The possibility of tetanus was considered. In some cases it is difficult to decide for a few days whether an elevation of temperature during or immediately after a serum eruption is due to a concealed complication

of the infectious disease for which serum was given or to the serum reaction. The presence of a leukocyte count below 12,000 or an eosinophilia is evidence in favor of serum disease as the cause of the temperature.

Mechanism

No attempt will be made here to offer a full discussion of the moot points concerning the underlying mechanism of serum disease. It has commonly been classed as an anaphylactic reaction, implying thereby that the reaction results from a union of antibody with its specific antigen. It has been supposed that during the incubation period, usually from six to twelve days, which follows a first injection of serum, antibodies are being formed, and that having attained the requisite concentration their union with the foreign serum still present in the circulation gives rise to the symptoms of serum disease. In this conception the reinjection of experimental anaphylaxis is unnecessary because the foreign serum is still present in the circulation and available for the reaction with antibody as soon as the latter has been formed in sufficient amounts by the body cells. The presence in the serum of the injected individual of specific precipitins for horse serum has been repeatedly demonstrated. Furthermore, it has been shown that in severe serum disease the titer of circulating precipitin is high and that those individuals who are insusceptible to serum disease are poor precipitin formers and continue to have the foreign serum in the circulation for several weeks after the time that it disappears from the blood-stream of those who have severe serum disease. Besides, it has been found that with the development of a high titer of circulating precipitin the precipitinogen disappears rapidly from the circulation. These observations on the relation of precipitin to the symptoms, coupled with the occurrence in most cases of an incubation period and the shortening of the incubation period upon reinjection, when from analogy with animal observations antibody would be expected to appear earlier, support the conception of serum disease as fundamentally dependent upon the union of an antibody with its antigen. Opposed to this viewpoint are the contentions that the desensitizing injections of experimental anaphylaxis are ineffective in human serum disease, that some cases of serum disease have an incubation period too short for the development of antibodies and that there are certain analogies between serum disease and drug idiosyncrasy, which presumably is not dependent upon an antigen-antibody reaction because of the non-antigenic nature of such substances. An obvious embarrassment for this point of view is that it implies a condition of hypersensitiveness to horse serum prior to the first injection in about 90 per cent of all individuals; and further it has no adequate explanation to offer for the many undoubted instances of a shocklike reaction upon reinjection of an individual who responded to the first injection only by a serum disease with the usual incubation period. For detailed discussion

of this problem the recent contributions of Coca and Doerr should be consulted.

Treatment

In a subsequent paragraph we shall discuss the prophylaxis and treatment of the alarming serum accidents in hypersensitive individuals. For the present we shall consider only what can be done to prevent or relieve the symptoms which occur after an incubation period in a non-allergic patient. In brief, little can be done beyond a certain measure of symptomatic relief. On the basis of its alleged property of altering cell permeability, calcium has been tried as a preventive, but the evidence that it diminishes by the methods of administration employed either the incidence or the severity of serum disease is not convincing. Kraus has reported a lower incidence of serum disease when diphtheria antitoxin prepared by immunizing goats instead of horses was used. Efforts to concentrate the serum so that the same amount of immune body is contained in a smaller volume of foreign protein have been successful in the preparation of diphtheria antitoxin, and one may hope that the total volume required of other types of serum will be similarly reduced.

One of the most interesting and constant phenomena of experimental anaphylaxis is the almost infallible effect of a desensitizing dose of the same antigen used in sensitizing. A serum sensitized guinea pig receiving a subcutaneous injection of 0.025 c.c. of the same serum becomes anti-anaphylactic and will then tolerate a dose otherwise quickly fatal. With this fact in mind it was expected that the symptoms of serum disease could be prevented by similar desensitizing injections. The anticipation has been falsified by numerous clinical observations and notably by those of Friedlander and Runnels.

For the pruritus during the period of eruption calamine lotion containing 1 per cent phenol is often helpful. Bicarbonate of soda baths sometimes give temporary relief. Benzyl alcohol, 4 per cent, either in solution or made up in an ointment with petrolatum and lanolin, relieves the pruritus in some cases. Temporary relief even in severe cases can usually be obtained by the subcutaneous injection of epinephrin, 0.3 to 0.7 c.c. (♏ v to ♏ x). Salicylates and the coal-tar derivatives are usually ineffective for the arthritis. The occasional very severe case may require morphin but usually the patient can be made tolerably comfortable by local heat and partial immobilization in cotton.

SERUM ACCIDENTS

From the pioneers in blood transfusion it was long ago learned that severe or even fatal effects might follow the parenteral introduction of

animal blood into man, but it was not until the advent of diphtheria antitoxin (1890) and the subsequent widespread practice of injecting human beings with horse serum that the significance of one form of such accidents was suspected. The literature since Bering's discovery contains many reports of tragic accidents following the injection of immunizing or therapeutic doses of diphtheria antitoxin. It was subsequently learned that in many of these cases the unfortunate individual had, prior to the serum injection, suffered from symptoms which we now recognize as due to horse allergy. Despite the greater prevalence of serum therapy in recent years, there have been fewer accidents, because the dangers are better understood and the recognition of those individuals liable to such accidents is now less uncertain.

Recognition and Classification of Individuals Liable to Serum Accidents.—Before administering a therapeutic serum one should invariably seek to elicit a history of asthma from any cause whatever and particularly a history of asthma or rhinitis from contact with horses. Often the horse asthmatic is well aware of the fact that driving behind a horse, riding, or entering a stable will bring on a paroxysm of asthma or the symptoms of an acute rhinitis and conjunctivitis, but there are also asthmatic patients, genuinely allergic to horse dander or horse serum, who have never been able to incriminate the horse definitely. The history should also include careful inquiry to learn of a previous serum treatment. It should be remembered, however, that patients who have received only an immunizing dose of diphtheria or tetanus antitoxin frequently do not recall this fact when coming under observation many years later.

It is perhaps emphasizing the obvious to state that the writer believes that serum should never be administered without first determining whether a cutaneous hypersensitiveness to horse serum exists. Of course, if serum from a species other than the horse be employed, skin tests with that serum should be done. For these skin tests the intracutaneous method is best. The skin of the forearm is cleansed with alcohol and approximately 0.02 c.c. of serum diluted 1:10 is injected *into* the skin. If properly done and the injection is intracutaneous and not subcutaneous a pale elevation 4 to 5 mm. in diameter appears with small depressions at the sites of hair follicles. Control tests with 0.85 per cent NaCl and normal human serum diluted 1:10 should be done at the same time. If, at the end of from ten to twenty minutes, the injection wheal has enlarged and a zone of erythema has formed around it, the reaction should be regarded as positive provided the control tests have not behaved in a similar way. The size of the wheal and the breadth of the surrounding erythema give a rough measure of the degree of cutaneous hypersensitiveness. In slightly positive reactions the wheal may measure only from 8 to 10 mm. and the erythema 20 or 25 mm.; in strong reactions the wheal may be 3 or 4 or more cm. in diameter and the erythema correspondingly

increased. Especially significant are the reactions in which the wheal shows projections like pseudopods, extending out into the surrounding zone of erythema.

Having obtained either a history of horse allergy or a positive skin test to horse serum the patient must be considered as one to whom serum can be administered only with the utmost caution. If there be a history of asthma or allergic rhinitis without relation to horses and a negative skin test, the danger of a severe reaction is less, but even in such cases caution is justified.

It is important to bear in mind that there are two groups of individuals hypersensitive to horse serum. In one the hypersensitiveness has developed spontaneously, usually in a person who has an heredity of allergy; other members of the family have had hay-fever, asthma, urticaria or eczema. In the other group the hypersensitiveness has been produced by a previous serum administration. In general the spontaneously hypersensitive manifest a much higher degree of allergy, and it is among this group that most of the fatalities have occurred. Indeed some of these patients are so exquisitely hypersensitive that even very minute amounts of serum may be disastrous. A case reported by Boughton will illustrate the extreme degree of allergy which may be encountered:

"A man, aged 29, who for the last 10 or 12 years had been subject to attacks of bronchial asthma when in proximity to horses, was anxious to have a desensitizing dose of horse serum, although he was familiar with the danger. He was taken to a hospital and 1 minim of horse serum was administered intravenously. Within 2 minutes a typical attack of asthma supervened. He was given 10 minims of epinephrin intravenously with definite relief for about 10 minutes. In all 50 minims of epinephrin were given in 5 doses, intravenously. Each gave relief for several minutes, but the patient died 45 minutes after the injection of serum."

In the following table an attempt has been made to classify the individuals who in known or unknown ways have become hypersensitive to horse proteins and it has further been attempted to arrange the groups and subgroups in the order of decreasing hypersensitiveness. Realizing that there are exceptions to the order given, it is, nevertheless, probably correct for the majority of individuals who are hypersensitive to horse serum or horse dander.

Classification of Individuals Hypersensitive to Horse Serum

I. Spontaneously hypersensitive.
   A. "Horse" asthmatics.
      1. Cutaneous reactions positive to both horse dander proteins and horse serum.
      2. Cutaneous reactions positive to horse dander proteins, but negative to horse serum.

B. Individuals with no history of asthma or previous serum treatment, but with a cutaneous reaction positive to horse serum.

II. Artificially sensitized.

A. Those to whom serum has been administered intraspinally.

B. Those to whom serum has been administered intravenously or into the tissues.

Since the spontaneously hypersensitive individuals are usually much more sensitive than the artificially sensitized, it is not surprising that most of the fatalities have occurred with patients in this group. Usually, the patient had been a genuine horse asthmatic or had had rhinitis and conjunctivitis from contact with horses. Sometimes he had had asthma but the incitant of the paroxysms was unknown; presumably some of these patients also were horse asthmatics without having detected the relation between horse dander and their symptoms. However, in addition to many reports of serious reactions after a second serum treatment given more than ten days after an uneventful first treatment, there are on record a few accounts of fatalities in patients who became sensitized by a previous serum treatment. Doubtless many unpublished cases have occurred. The writer has personal knowledge of three. It is, of course, well known that many individuals after a serum injection either do not become sensitized or quickly lose their allergy. This is unquestionably true of those receiving small amounts of serum subcutaneously or intramuscularly as in diphtheria and tetanus immunization. But it is not so certain that many escape sensitization after large amounts are administered intravenously or intraspinally. In fact recent observations indicate that most pneumonia patients treated with serum in amounts over 100 c.c. retain for years a cutaneous allergy to horse serum. The concomitance of a cutaneous allergy and a general allergy is sufficiently frequent to make such a patient potentially a dangerous subject for subsequent serum therapy. These artificially sensitized individuals can, however, in most cases be given serum in therapeutic amounts if proper precautions, to be discussed presently, are observed. They are, to be sure, usually much less sensitive than the "horse" asthmatic but nevertheless caution in giving them serum is abundantly warranted from past clinical experience.[2]

Symptomatology.—There is a striking uniformity in many of the clinical records of the early serum fatalities. Often the victim, in perfect health, had come to the physician for an immunizing dose of diphtheria antitoxin. Almost before the needle was withdrawn there was local edema

[2] The reports of sudden death following the administration of serum to individuals belonging to the status lymphaticus group justify caution in using serum therapy on patients who are unquestionably of this type. Just how much danger there is in such cases is not clear, but the writer believes that serum, if it is to be administered in considerable quantities, should be given in divided doses.

and itching and a feeling of apprehension followed quickly by generalized giant urticaria, often sneezing and a prickling sensation in the throat, edema of the face, hands and neck or perhaps of the whole body, cyanosis, choking sensation, cough, violent asthma, dilated pupils, sweating, disappearance of radial pulse, convulsions and death within from five to ten minutes. Less fulminating cases in which death is postponed for several hours are also on record. The cases in which the fatal injection was made intrathecally have given a somewhat different clinical picture, but usually if the patient lives an hour he makes a complete recovery. In non-fatal cases the symptoms often subside rapidly after an hour or two and the patient may feel quite well the next day except for a residual urticaria; in others following the immediate shocklike reaction the patient may have symptoms for several days quite similar to those of the usual serum disease, or there may be complete recovery from the immediate reaction and then after an incubation period of from three to seven days the common form of serum disease.

Prophylaxis of Serum Accidents.—An important portion of the prophylaxis of serum accidents has already been considered in discussing the identification of those who are hypersensitive to horse serum. Previous symptoms of allergy or a history of some form of serum therapy or a positive skin reaction to horse serum should put one on his guard. As has been said, the degree of hypersensitiveness can be roughly estimated from the history and from the intensity of the skin reaction.

The other phase of the prophylaxis of serum accidents is *desensitization.* Having learned that the patient in need of serum is hypersensitive to horse serum, how much can be done so to increase his tolerance that therapeutic amounts may be safely given? Probably most of those whose allergy to horse serum dates from a previous serum administration can in the course of from twelve to twenty-four hours attain sufficient desensitization to tolerate large amounts, but certainly some of the spontaneously hypersensitive cannot be given more than minute amounts without grave danger. It should be clearly recognized, therefore, that, despite efforts toward desensitization, serum therapy for some patients is impossible. It has often been stated that a desensitizing dose of 0.5 c.c. or 1.0 c.c. should be given subcutaneously before the whole quantity is administered. While this may be helpful in some cases, it is totally inadequate for the individual with more than a slight degree of hypersensitiveness and extremely dangerous for individuals with the exquisite hypersensitiveness of some "horse" asthmatics. Besredka introduced a method by which he believed desensitization could be accomplished in any patient. It consists of giving intravenously at intervals of from two to ten minutes increasing doses of serum, beginning with 1 c.c. of a 1:7 dilution. Despite the fact that Besredka's early estimate of the method, based apparently on animal experiments, was overenthusiastic,

it forms the basis of the methods which, so far as is known, offer the best hope of desensitization. It should be remembered that desensitization in man is not accomplished with the rapidity, certainty or completeness characterizing the process in the guinea pig. Apparently, also, individuals vary considerably in their susceptibility to serum desensitization.

The literature of serum desensitization in man does not contain sufficient data to enable one to outline with complete confidence a program to cover all cases, but past experience makes it seem highly probable that the dosage and intervals stated below may be followed in almost all patients hypersensitive to horse serum. If the patient has had asthma and gives a positive skin test the first desensitizing doses should be given subcutaneously, beginning with a dose of 0.005 c.c. to 0.025 c.c., according to the intensity of the skin reaction. The dose should be doubled every thirty minutes until 1 c.c. is given. Then 0.1 c.c. is given intravenously. After twenty minutes the dose is doubled. In case the therapeutic serum is to be given intravenously in large amounts, the intravenous injections are continued, the dose being doubled every twenty to thirty minutes until 25 c.c. has been given without reaction. Four hours later 50 c.c. may be given and after eight hours the treatment may be continued in the usual manner. In case anything more than a mild reaction occurs, one should wait the usual interval, and then the last dose which gave no reaction or only a mild one is repeated. There is no evidence suggesting a cumulative action. The first portion of the serum should always be given very slowly and careful watch kept for the symptoms of serum accidents. In case the serum is to be administered intraspinally, the subcutaneous doses should be carried out in the same way and five or six of the intravenous doses given, when, if there has been no reaction, the intraspinal route with diluted serum may be tried very cautiously.

As for the patient who has previously been treated with serum, and is demonstrably hypersensitive by the skin reaction, the same procedure should be followed. However, unless the cutaneous allergy is very marked, the first dose may be from 0.02 c.c. to 0.05 c.c. and it is probably quite safe with some of these less sensitive patients to shorten the desensitization program in case the first few injections produce no reaction. This may be done by increasing the doses a little more rapidly than by doubling the preceding amount. The first intravenous dose, to be on the safe side, should never be more than one-tenth of the largest subcutaneous dose producing no symptoms. One cannot emphasize too strongly the importance, in any attempt at desensitization, of having at hand ready for use a syringe containing epinephrin.

Treatment of Serum Accidents.—For any shocklike reaction during or after serum administration epinephrin is a specific. In mild reactions without alarming symptoms a hypodermic injection of from 0.3 c.c. to

0.8 c.c. (♏ v to ♏ xii) will usually prove effective, repeated after twenty or thirty minutes if necessary. For the more severe reactions, doses of 0.7 c.c. to 1 c.c. (♏ xi to ♏ xvi) should be given and if necessary repeated. Only in the very grave reactions with death apparently imminent is intravenous administration of epinephrin indicated and in such cases it is probably better to repeat injections of from 0.5 c.c. to 0.7 c.c. (♏ viiss to ♏ xii) rather than a single or a few large doses. The first dose, however, in such a crisis might justifiably be, for an adult, 1 c.c. (♏ xvi).

In addition to epinephrin, atropin gr. 1/60 to gr. 1/30 subcutaneously may be given in severe cases. It is not clear just how effective morphin is in these reactions, but it is probably of some usefulness in preventing the recurrence of symptoms after epinephrin has carried the patient through the immediate crisis. Artificial respiration should be employed, of course, in alarming cases.

REFERENCES

Besredka, A. Anaphylaxie et Antianaphylaxie, Paris, Masson et Cie., 1917.

Boots, R. H., and Swift, H. F. The Arthritis of Serum Sickness, Journ. Am. Med. Ass., lxxx, 12, 1923.

Boughton, T. H. Anaphylactic Death in Asthmatics, Ibid., lxxiii, 1912, 1919.

Coca, A. F. Hypersensitiveness, Tice's Practice of Medicine, New York, W. F. Prior Co., 1920.

Coca, A. F., Deibert, D., and Menger, E. F. On the Relative Susceptibility of the American Indian Race and the White Race to the Allergies and to Serum Disease, Journ. Immunol., vii, 201, 1922.

Currie, J. R. On the Supersensitization of Persons Suffering from Diphtheria by Repeated Injections of Horse Serum, Journ. Hyg., vii, 35, 1907.

Dale, H. H., and Hartley, P. Anaphylaxis to the Separated Proteins of Horse Serum, Biochem. Journ., x, 408, 1916.

Doerr, R. In Kolle u. Wassermann, Handb. d. path. Mikroörg., 2d ed., ii, 947, 1912-1913.

——— Die Anaphylaxieforschung, Ergebn. d. Hyg., v, 71, 1922.

Dreyfuss, J. Serumtod infolge von Anaphylaxie, München. med. Wchnschr., lix, 198, 1912.

Friedlander, A., and Runnels, S. C. Reaction Following Use of Antipneumococcic Serum, Mil. Surgeon, xlii, 320, 1918.

Gewin, J. Chlorkalzium gegen die Serumkrankheit, München. med. Wchnschr., lv, 2670, 1908.

Gilette, H. F. Untoward Results from Diphtheria Antitoxin with Special Reference to Its Relation to Asthma, N. Y. State Journ. Med., ix, 373, 1909.

Goodall, E. W. Serum Sickness, Lancet, i, 323, 1918.

Gottstein, A. Uber Todesfälle welche bei der Anwendung des Diphtherie-Heilserums beobachtet worden sind, Therap. Monatsh., x, 269, 1896. 1896.

Hutinel, V. Sérothérapie et anaphylaxie dans la Méningite cérébro-spinale, Presse méd., xviii, 497, 1910.

Koch, W. Beitrag zur Kenntnis der Serum Anaphylaxie beim Menschen und deren Verhütung, Berl. klin. Wchnschr., lii, 685, 1915.

Kraus, R., Cuenca, B., and Sordelli, A. Uber die Verhütung der Serumkrankheit durch Anwendung des Diphtherie—und Tetanus-serums von immunisierten Rindern, München. med. Wchnschr., lxviii, 1244, 1921.

Longcope, W. T., and Rackemann, F. M. The Relation of Circulating Antibodies to Serum Disease, Journ. Exper. Med., xxvii, 341, 1918.

Mackenzie, G. M. Serum Desensitization, Journ. Am. Med. Ass., lxxvi, 1563, 1921.

Mackenzie, G. M., and Leake, W. H. Relation of Antibody and Antigen to Serum Disease Susceptibility, Journ. Exper. Med., xxxiii, 601, 1921.

Mason, V. R. Optic Neuritis in Serum Sickness, Journ. Am. Med. Ass., lxxviii, 88, 1922.

Nemmser, M. Wiederholte Seruminjektionen und Ueberempfindlichkeit, Deutsche med. Wchnschr., xxxix, 740, 1913.

Ohnacker, H. Zur Aetiologie und Prophylaxie der Serumkrankheit, Zentralbl. f. inn. Med., xxxi, 1206, 1910.

Park, J. H., and Chickering, H. T. Type I Pneumococcus Lobar Pneumonia among Porto Rican Laborers, Journ. Am. Med. Ass., lxxiii, 183, 1919.

Pirquet, von, C. F., and Schick, B. Die Serumkrankheit, Leipzig und Wien, 1905. Deuticke.

Rackemann, F. M., Longcope, W. T., and Peters, J. P. The Excretion of Chlorides and Water and the Renal Function in Serum Disease, Arch. Int. Med., xviii, 496, 1916.

Rolleston, H. D. Serum Disease after Intrathecal Injections of Serum, Lancet, ii, 821, 1917.

Schippers, J. C., and Wentzel, J. M. Zur Behandlung der Serumkrankheit, Zentralbl. f. inn. Med., xxxi, 697, 1910.

Weaver, G. H. Serum Disease, Arch. Int. Med., iii, 485, 1909.

CHAPTER IV

ANAPHYLACTIC FOOD POISONING

I. Chandler Walker

Definition of Anaphylaxis.—Magendie, in 1839, and Richet, in 1902, found that the first dose of a protein given to an animal was followed by a condition of markedly greater susceptibility to that protein. This phenomenon is called anaphylaxis; the animal is sensitized by the first dose of protein and is shocked by a properly spaced second dose of that protein. The anaphylactic shock is due to the meeting of a specific antigen (the second dose of protein) with its antibody (produced by the first dose) and the resulting reaction gives rise to a toxic product which causes the characteristic symptoms. Anaphylaxis therefore consists simply in the cellular reaction due to the fixation of antigen by cellular antibody. Anaphylaxis is then the reverse of vaccination or immunization since the anaphylactic animal reacts to the second injection much more strongly than to the first. With the human the word "allergy" is often used for protein sensitization.

In the chapters on Bronchial Asthma and Hay-fever, the part played by protein sensitization or anaphylaxis in the cause of these conditions has been described and it is in these conditions that protein sensitization is most common. There are, however, other conditions or diseases the symptoms of which are more or less often caused by anaphylaxis and the cutaneous or skin test should be used to determine whether or not and what proteins are the cause.

Eczema.—In infants chronic eczema exclusive of the scalp alone is very frequently due to some food protein even while the infant is being breast fed. Rarely do breast-fed infants show sensitization to human milk but, when this is the case, goat's milk may be substituted. Usually the nursing infant is sensitive to some protein that he has never eaten but that the mother is eating in large quantities, such as cow's milk, egg, cocoa, etc. The human milk in such instances contains the food protein which the child has ingested and absorbed. Even though the mother is not sensitive to these proteins, the nursing infant may be and, therefore, the nursing infant should be tested with the proteins which the

mother is eating. Treatment naturally consists in the omission from the mother's diet of the protein that affects the child.

In children eczema is frequently caused by some food protein that the child is eating. When eczema begins at the period of weaning, as is very often the case, the cause is usually the proteins of milk, egg, white flour, oat or potato, since these are the first to be eaten in much quantity and are, so to speak, foreign proteins to the child. When eczema develops in older children, the above-mentioned food proteins are less often the cause, and other foods, such as tomatoes, strawberries, and in fact any food that the child eats, may be the cause. Therefore the older the child when eczema begins, the less frequent are foods the cause and the larger must the list of food proteins be for determining the causative one by the cutaneous test. Treatment consists of omission of the offending protein as determined by the cutaneous test.

In adults, food proteins are rarely the cause of eczema; however, if the eczema is not amenable to the usual treatment and no cause is demonstrable by other means, food protein tests are worth trying.

Since this chapter concerns only anaphylactic foods, other causes of eczema should not be mentioned; however, since fats and carbohydrates are foods and at times cause eczema in children and adults, even though they are not anaphylactic because they are not proteins, it may not be amiss to mention fats and carbohydrates as a cause of eczema. In about 20 per cent of a series of eczema cases studied by O'Keefe, there appeared a lowered fat digestion shown either in the form of free fat or as a definite excess of soap in the stools, and in about 10 per cent there was evidence, either clinical or laboratory, of a carbohydrate indigestion. Furthermore it may be mentioned that the author has occasionally found eczema to be due to bacteria (Staphylococcus aureus), to pollens (grass and ragweed) and to animal emanations. In these latter cases treatment should be given respectively, with Staphylococcus aureus vaccine, pollens or animal hair proteins, as the case may be, as determined by cutaneous tests with these proteins. Locally crude coal-tar is probably the best medication.

Urticaria.—Urticaria or hives is frequently, though less often than eczema, caused by food proteins. Not only are the common or frequently eaten foods the cause, but also foods, such as strawberry and shellfish, that are eaten less often or at definite seasons. Therefore, cutaneous tests should be done with a wide range of food proteins.

Specific Treatment.—Usually omission of the offending proteins brings relief; however, occasionally an urticaria that is definitely caused by a food will persist for unknown reasons over a long period of time or will recur at intervals even though the causative protein has not been eaten. Similar instances are frequent following the injection of therapeutic serums. Urticaria is occasionally a complication in the treatment

of hay-fever and asthma; the injection of too large doses of the pollen or animal emanation protein may cause an urticaria of a few hours duration, but it does not become chronic or recurrent.

Non-specific Treatment.—Frequently urticaria, from the history of the patient or for some other reason, seems to be caused by foods when the protein tests are negative. Vallery-Radot calls this digestive or alimentary urticaria and treats the condition by feeding capsules of peptone in 0.1-gm. doses one-half to one hour before each meal. This treatment is based on the theory that peptone is an early decomposition product of all proteins and by giving it prior to the ingestion of food the patient is made temporarily anti-anaphylactic or non-sensitive to any food protein so that the eating of the causative food, whatever it may be, will not produce urticaria. The author has obtained better results by giving Bacillus acidophilus with milk sugar in milk prior to each meal than by giving peptone. Small doses of milk of magnesia prior to each meal seem to be of considerable benefit. Bacillus acidophilus and milk of magnesia seem to speed up the gastro-intestinal tract, thereby diminishing the chance of absorption of undigested proteins which probably cause this type of urticaria. Free evacuation of the intestinal tract is desirable.

Angioneurotic Edema.—That which has been stated above for urticaria is equally true for angioneurotic edema.

Conjunctivitis.—Conjunctivitis unaccompanied by any other manifestation and stubborn inflammations of the conjunctivæ recurring in the same patient at or about the same time year after year is frequently due to food proteins. Conlon, who was the first to observe and publish such a condition, found that his patients gave a positive skin test with egg, sole, tomatoes and strawberries, and the omission of these foods was followed by relief. Conlon believes that, in the absence of uncorrected ametropia, all recurring low-grade inflammation of the conjunctivæ which the patient calls "frequent attacks of red eyes" should be considered as possibly due to food anaphylaxis.

Gastro-intestinal Symptoms.—Abdominal pain and cramps with nausea, vomiting, bloating and indigestion are infrequently due to protein sensitization. Occasionally abdominal pain is the only or most striking symptom and rarely the patient may become unconscious following indigestion symptoms due to food proteins. The cutaneous test usually shows the offending protein but sometimes, when this test fails, the intracutaneous test will determine the cause.

Duke has studied a number of patients who had gastro-intestinal symptoms due to eating egg, shad roe, milk, beef, pork, honey, strawberries, lettuce, almond, bean, potato, onion, cabbage, rice and tomato. The pain appeared soon after the ingestion of the food and lasted from three to six hours; occasionally the pain appeared later and lasted longer. This condition is more frequent in individuals who have organic lesions in the

gastro-intestinal tract. Treatment naturally consists of omission of the offending protein to prevent future attacks, and for the acute attack gastric lavage, purgation and adrenalin subcutaneously should be employed.

Bladder Symptoms.—Duke was the first to call attention to the fact that some patients who have frequent painful urination or constant pain over the bladder, the severity of which is all out of proportion to the lesions revealed by careful urological examination, may be sensitive to some food protein. In fact, Duke believes hypersensitiveness to proteins is a relatively common cause of bladder symptoms in those patients who exhibit little or no pathology in the urinary tract. These patients frequently have other protein sensitivity conditions, such as urticaria, angioneurotic edema or asthma, and the bladder symptoms are part of a general reaction to the protein sensitivity. The cutaneous or intracutaneous test with food protein usually determines the cause. Treatment consists of avoidance of the particular protein, the administration of adrenalin if necessary, and the removal by the urologist of contributory factors, such as polypus, caruncle, cystitis, etc., if any be present.

There are other diseases or conditions due to food poisoning but, since at present there is no evidence that anaphylaxis plays a part, they need not be mentioned in this chapter.

REFERENCES

Conlon, F. A. Am. Journ. Ophth., ii, 486, 1919.
Duke, W. W. Arch. Int. Med., xxviii, 151, 1921.
——— Ann. Clin. Med., i, 117, 1922.
O'Keefe, E. S. Journ. Am. Med. Ass., lxxviii, 483, 1921.
Shannon, W. R. Am. Journ. Dis. Child., xxii, 223, 1921.
Vallery-Radot, Pasteur. Ann. de méd., viii, 303, 1920.
Walker, I. C. Journ. Am. Med. Ass., Study xviii, lxx, 897, 1919.

CHAPTER V

THE VISCERAL MANIFESTATIONS OF THE ERYTHEMA GROUP OF SKIN LESIONS

George Blumer

Over a hundred years ago the English dermatologist Willan noted that attacks of erythema might be accompanied by visceral manifestations, but this association was not widely recognized until after the appearance of Henoch's article in 1874 and the various contributions of Osler published between 1895 and 1914.

It is assumed that this group of phenomena is anaphylactic in nature, though there is no definite proof of this. It is clear that the picture may follow infection, as Saisawa and others have shown, but it is also clear that no such etiology is apparent in many patients and this latter class of cases Osler describes as of metabolic origin.

The characteristic features of the disease are the occurrence of attacks of an exudative skin lesion with visceral manifestations. The skin lesions may be absent in some attacks, and identical skin lesions may occur without visceral symptoms.

The striking feature of the skin lesions is their polymorphism. They may take the form of purpura, of urticaria, of simple erythema, of nodose erythema, of angioneurotic edema or of necrotic bullous lesions. In the same patient different types of skin lesion may occur in different attacks or in the same attack.

According to Osler the visceral manifestations are of two kinds, the exudative and the inflammatory. The latter may be dismissed in a few words as they are essentially the lesions which may occur as secondary phenomena in many infectious processes, namely: pericarditis, endocarditis, pneumonia, or nephritis. The arthritis which occurs in many patients is probably an exudative rather than an inflammatory process and this is doubtless true in some instances of the renal changes.

Symptoms.—The most common exudative visceral changes affect the gastro-intestinal tract and give rise to a clinical picture of acute diffuse abdominal pain, usually occurring at night, associated with vomiting and at times with fever. There may be hematemesis and in some patients diarrhea with bloody stools. The absence of muscle spasm in most patients is of great diagnostic importance, for an erroneous diagnosis of acute surgical abdomen is likely to be made, particularly if the skin lesions are inconspicuous or absent and if the past history is not carefully considered.

Next to the gastro-intestinal lesions the nephritic are the most common and these range in severity from a transient albuminuria, almost surely an exudative phenomenon, to severe and intractable nephritis resulting in death.

Of less importance are hemorrhages from the mucous membranes, cardiac complications, transient paralyses from cerebral exudation or true hemorrhage and respiratory involvement in the form of bronchitis or pneumonia.

Arthritis occurs in about 40 per cent of the patients. The mortality of all forms is a trifle over 20 per cent.

Treatment.—Little in the way of treatment, beyond symptomatic treatment, has so far been suggested. For the acute attacks adrenalin in the form of the standard 1 : 1,000 solution should be given intramuscularly in doses of from 10 to 15 minims. Osler suggests nitroglycerin in patients with angioneurotic edema. Skin tests for hypersusceptibility to various proteins should be carried out and desensitization should be attempted if an abnormal susceptibility is detected. In the case of food susceptibility the offending article should be eliminated from the diet until the individual is desensitized. Local foci of infection should be removed. Osler claims to have obtained favorable results in some patients with arsenic and in others with alterative doses of gray powder and careful dieting.

Symptomatic treatment is likely to be needed in the abdominal cases on account of pain. In some instances this may be severe enough to demand morphin hypodermically. Local applications of heat may be comforting to the patient. The diet during the acute stage in patients where vomiting is a prominent feature should be liquid, easily digested and minimum in amount; indeed temporary withdrawal of nourishment may be necessary. Various gastro-intestinal sedatives such as bismuth, cerium or even cocain in small doses may be employed. In view of the frequency of renal lesions, an attempt should be made to supply an adequate fluid intake, if necessary by the bowels or by intravenous infusion of normal saline. The cardiac, renal and cerebral manifestations should receive the usual treatment as discussed under the appropriate sections elsewhere in this work.

REFERENCES

Christian. Journ. Am. Med. Ass., lxix, 325, 1917.
Foster. Journ. Cutan. Dis., xxxiv, 808, 1916.
Morrison. Boston Med. & Surg. Journ., clxxi, 65, 1914.
Osler. Am. Journ. Med. Sc., cx, 629, 1895; cxxvii, 1, 1904.
——— Brit. Journ. Dermat., xii, 227, 1900.
——— Brit. Med. Journ., i, 517, 1914.
Saisawa. Deutsche med. Wchnschr., xxxix, 792, 1913.

DISEASES DUE TO DIETARY DEFICIENCIES

CHAPTER VI

BERIBERI,[1] NUTRITIONAL EDEMA AND EPIDEMIC DROPSY

H. Gideon Wells and Samuel T. Darling

BERIBERI

Modern development of our knowledge of the fundamentals of nutrition has taken beriberi from the place it formerly occupied among the diseases of unknown etiology, and has placed it in the group of food deficiency disorders, at the same time solving most of the problems of its prevention and curative treatment. The rapid accretion in knowledge concerning the essential accessory food substances has, in return, owed much to the study of beriberi for its progress, since it was in the reinvestigation of Eijkman's pioneer observations on an experimental "illness of fowls similar to beriberi" that Casimir Funk developed the concrete idea of essential, hitherto unrecognized dietary necessities, for which he coined the name "vitamines."

Although many clinical observers had recognized the relationship of faulty diet to beriberi, the evidence obtained from human material was, as is usually the case, complicated by too many other factors to make the dietary relationship altogether convincing. Even the clear-cut experiment of Fraser and Stanton—who, in 1907-1908, found that in Javanese laborers isolated in a virgin jungle, those who were fed polished rice developed beriberi and those who were fed unpolished rice escaped—controlled as it was by reverse experiments with the same subjects, failed to carry conviction because there were so many clinical and epidemiological observations that indicated an infectious or a toxic etiology. Not until the disease had been produced in its essentials in experimental animals did it become possible so to control the conditions that the true etiology could be demonstrated in a convincing manner. This necessary step we owe to the Dutch physician, C. Eijkman, who in 1897 reported his studies with the following introductory statement:

[1] A complete review with bibliography to 1913 is given in the monograph, Beriberi, by Edward B. Vedder. More recent literature concerning the vitamin and other nutritional aspects will be found in the monographs on the vitamins, which are cited in the references.

"It is now some years since I first noticed in Batavia for the first time a disease of fowls, which, because of its striking resemblance in many respects to the human beriberi, at once aroused my interest and occupied my continued study almost uninterruptedly until my return to Europe."

This condition, which is now usually referred to as polyneuritis gallinarum, he found could be produced at will by feeding the fowls on polished rice, and it could be cured or prevented equally well by feeding an extract of the rice polishings. The degenerative changes in the nervous tissues, charactistic of both beriberi and polyneuritis gallinarum, he attributed to poisons resulting from the excessive proportion of starch in the diet; and the curative effect of rice polishings he thought was accomplished by a neutralization of the hypothetical metabolic poisons by some constituent of the outer layers of the rice grains. Therefore, although he put the study of the disease upon an experimental basis and proved its dependence on a polished rice diet, he failed at first to recognize that it depends solely on a deficiency in the diet. In 1906, however, he published the statement that there is present in rice polishings a substance which is not protein, carbohydrate, fat or salts, the lack of which causes "nutritional polyneuritis," whereby he definitely established the existence of essential dietary constituents different from the known foodstuffs. Although his work was unnoticed for some years, he is now recognized as one of the most important pioneers in the study of vitamins, and as the one who first established the true nature of beriberi as a deficiency disease.

Other steps of importance in our knowledge concerning the etiology of beriberi may be summarized briefly as follows: In 1901, another Hollander, Grijns, found that experimental polyneuritis in fowls can be prevented by adding beans to the diet (he used Phaseolus radiatus) and a countryman, Hulshoff-Pol, 1902, found them equally effective in the prevention and treatment of human beriberi. These men were stimulated to this work by the prevalence of beriberi in the Dutch Indies, and for a similar reason American investigators undertook work in the Philippines, and the British in their Asiatic territories.

In 1907, Fraser and Stanton reported that by extracting rice polishings with weak alcohol they secured a product which cured beriberi in human subjects, thus completing the clinical evidence which their experiment on the Javanese laborers had furnished, that a diet chiefly of polished rice is, of itself alone, able to produce human beriberi.

Chamberlain and Vedder, in 1911, corroborated the experimental and clinical observations of the Dutch and British investigators, finding that both adult and infantile beriberi can be cured by extracts of rice polishings, and extended our knowledge of the active agent. This they found to be soluble in water and alcohol, dialyzable, moderately resistant to

heating, more stable in neutral and weak acid than in weak alkaline solutions, and, as far as they could determine, not identical with any well-known constituent of foods. Funk, in the same year, published his studies on the nature of the antineuritic substance, which he believed to be a combination of nicotinic acid with a pyrimidin base. Although he was in error in believing that he had identified the active agent, he made the prediction that other hitherto unknown substances would be found to bear the same relation to other deficiency diseases, and coined the name "vitamine," believing these substances to be "amines" essential for life.

Although this name is technically incorrect, since the active agents are probably not "amines," yet it has been generally adopted. The chemists have taken the sting from it, as far as chemical terminology is concerned, by deleting the final *e*, thus removing the evidence that it signifies an "amine." Through a series of events of no consequence in this discussion, it has come to be identified closely with the vitamin B, which is the name often given to it in literature on nutrition, although, as the identity of the antineuritic vitamin with the growth-promoting vitamin B is by no means established, this terminology is not fully justified.

The Antineuritic Vitamin

Despite numerous attempts since the studies of Funk (and of Suzuki, who also produced an active product at about the same time), this vitamin has not been isolated and its nature remains unknown. It is not even certain whether it is identical with the growth-promoting vitamin B, with which it is usually associated and from which a positive separation has not been made. The chemical properties that are known are these: antineuritic vitamin is readily soluble in water and in alcohol under 70 per cent strength, not readily soluble in fat solvents, strongly held by adsorptive substances such as Fuller's earth and animal charcoal, diffusible through membranes, relatively stable to heat and oxidation, especially when in weakly acid solution in which it will stand boiling for an hour. There is some reason to believe that it is a nitrogenous base related to the purins or pyrimidins.

The effects of deficiency in antineuritic vitamin seem to be essentially the same in birds, man and other mammals. Apparently on usual dietaries there is a considerable reserve supply in the tissues, so that after removal of all vitamin from the food there is a latent period before the effects of the deficiency are manifested. McCarrison has found that the tissue changes that result from such a diet are altogether similar to those of starvation, there being a reduction of weight in nearly all tissues except the adrenals which are much hypertrophied; there is loss of weight, fall in temperature, slowing of respiration and reduced resistance to infection. Starvation does not lead to neuritis or beriberi because the subject does

not live long enough; nevertheless, the nerve tissues may show more or less of the same sort of degenerative changes that are seen in the early stages of beriberi or polyneuritis. There is a marked loss of appetite which may be an important factor in the progress of the deficiency. Even in experimental animals heart weakness with sudden death is often seen, thus carrying out the resemblance of the experimental disease to human beriberi. There is some evidence that a high proportion of carbohydrate in the deficient diet increases the effect of the vitamin deficiency, which explains the common relation of beriberi to diets composed chiefly of polished rice or white flour. Especially is there reason to believe that the wet form of beriberi depends on a relative excess of carbohydrates, as seen in famine edema or war dropsy. Other things being equal, an excessive demand for continued muscular activity in a person deficient in vitamin will favor appearance of the manifestation of the deficiency, and hence beriberi may appear in soldiers and sailors accomplishing heavy tasks when it does not appear in the general population on the same diet. Likewise, pregnancy and lactation often precipitate beriberi in mothers, whose children may also exhibit the same disease.

Vedder has advanced the hypothesis that the antineuritic vitamin must be a substance needed for the repair of nervous tissue, so that in its absence the normal wear and tear losses cannot be made good. The paralysis, he believes, depends more on central than on peripheral nerve changes, since the degeneration of the nerves precedes the paralysis and may persist long after the paralysis has disappeared. As rice polishings relieve the cardiac symptoms, which are important features of beriberi, it is to be assumed that the vitamin is essential for the heart metabolism. Furthermore, heart muscle contains vitamin which will protect from polyneuritis birds fed on polished rice. This does not seem to be identical with the vitamin isolated by Funk, for, while it relieves the cardiac symptoms and dispels the dropsy of wet beriberi, it does not cure the paralytic symptoms of dry beriberi, according to Vedder. This author "has a growing belief that dry and wet beriberi are separate and distinct diseases, which are, however, generally associated." Rice polishings, he says, clear up beriberi dropsy quickly, but do not affect the paralysis unless the polishings have been hydrolyzed.

Certain it is that beriberi is a deficiency disease seldom seen except in those whose chief article of diet is rice with its high carbohydrate content. In this respect it may be compared with pellagra which seems also to be a deficiency disease, but which occurs chiefly among people whose staple food is maize. We do not commonly see beriberi among the pellagrous peasants of Roumania and Italy, nor do we often see pellagra among the people of Java and the Philippines. Isolated cases of either disease may appear anywhere that suitable arrangement or utilization of foodstuffs produces the proper dietary deficiency, and presumably this may

occur sometimes in unexpected places and under circumstances difficult of explanation. But taken by and large, beriberi is a disease of rice eaters, and pellagra attacks the eaters of maize. The principal endemic foci of beriberi are in Asia, involving especially Japan, the Philippines, the Dutch Indies, the Malay States and parts of China; in Africa, affecting chiefly the coast regions and the adjacent islands; and in South America, especially Venezuela, the Guineas, Brazil, Paraguay and Uruguay. However, numerous epidemic-like outbreaks and isolated cases have been observed in all parts of the world, especially among inmates of asylums and prisons, and in seamen. The fishermen of Labrador and Newfoundland, who live chiefly on white flour during part of the year, have furnished numerous cases of beriberi.

Treatment

Prophylaxis is of necessity by far the most important feature of the treatment of this disease, and is essentially a matter of diet. So widespread is the antineuritic vitamin that it is not difficult ordinarily to prevent beriberi, and also the less obvious manifestations of vitamin deficiency, if only the need for a suitable diet is known. Any diet that is not predominatingly carbohydrate is usually safe, as far as beriberi is concerned, and any carbohydrate diet that does not consist chiefly of artificially milled grains deprived of their outer coverings will not induce beriberi in its frank manifestations. The early observations by Takaki in the Japanese Navy showed that so simple a measure as replacing part of the polished rice in the ration by barley is sufficient to prevent the disease. An imposing list of foods in which the antineuritic vitamin has been demonstrated is given by Sherman and Smith, by Eddy, and other writers on the vitamins. Richest in the antineuritic vitamin among ordinary foods are millet, peas, beans, green vegetables of practically all kinds, most fruits (grapes and bananas are relatively poor), all fresh meats (but especially viscera as compared with muscle), milk, eggs, nuts and whole grains with the germ included. Oils, fats, butter, cheese, lean muscle and meat extract are either totally devoid of or very poor in the necessary vitamin. Fortunately it is more resistant to ordinary cooking temperatures than is the antiscorbutic vitamin, and hence uncooked foods are not necessary for prevention. Likewise it resists oxidation well, and is stable in solutions that are acid or neutral, though alkaline solutions are injurious. In culinary preparation loss is more likely to occur through the water solubility of vitamin B in processes in which the cooking water is discarded. With the degree of heat used in commercial canning and in some processes of desiccation and sterilization, serious losses may occur, and hence an exclusive diet of canned food is hazardous, although under such circumstances scurvy is more to be feared.

In view of the fact that all but a few of the ordinary foods contain an abundance of vitamin B, obviously to know the danger of beriberi insures its avoidance. Only a peculiarly limited and artificial diet can produce this particular disease, and only extreme poverty or compulsion leads people to a diet that will cause it.

In prisons and other institutions where restricted and monotonous diet might lead to beriberi, the following simple rules laid down by Vedder should be observed, for they will insure in a simple but adequate way the prevention of this as well as other deficiency diseases:

In any institution where bread is the staple article of diet, it should be made from whole wheat flour.

When rice is used in any quantity, the brown undermilled, or so-called hygienic, rice should be furnished.

Beans, peas or other legumes, known to prevent beriberi, should be served at least once a week. Canned beans or peas should not be used.

Some fresh vegetables or fruit should be issued at least once a week and preferably at least twice a week.

Barley, a known preventive of beriberi, should be used in all soups.

If cornmeal is the staple of diet, it should be yellow meal or water-ground meal, that is, made from the whole grain.

White potatoes and fresh meat, known preventives of beriberi and scurvy, should be served at least once a week, and preferably once daily.

The too exclusive use of canned goods must be carefully avoided.

Universal prevention of beriberi will be readily enough attained by legislative action which effectively prohibits the preparation and sale of overmilled grains, reduced in food value, poor flavored, and inferior to the whole grain in most respects except keeping qualities.

The suitability of a given rice supply for prevention of beriberi depends upon the extent to which the outer coats have been removed, and this is easily determined. As the outer layers contain most of the phosphorus of the grain, chemical analysis gives good evidence of the extent to which milling has been carried, a phosphorus pentoxid content of 0.4 per cent or more indicating a safe degree of undermilling. Or if the rice grains are stained with Gram's iodin solution, the remaining portions of the external layers will prevent the iodin staining the starch blue; an overmilled rice stains deep blue, a safe rice shows most of the surface unstained (Vedder).

Curative Treatment.—The principle of treatment in developed cases of beriberi must be the prompt restoration of the lacking vitamin, in order to prevent further damage and to facilitate the maximum degree of recovery that the extent of destruction of nerve tissue permits. In severe acute cases the dramatic improvement observed in polyneuritic fowls may

be achieved with man. Vedder cites the case of a patient with chronic beriberi suffering from an acute cardiac crisis which seemed about to terminate fatally in a few hours, but which was immediately relieved by oral administration of extract from rice polishings. He says that similar results have been obtained in other cases, and it has also been found that cases of wet beriberi may be just as promptly cured in this manner. Large effusions disappear in the course of a few days after the use of the extract is commenced. Its use is therefore recommended in cases of wet beriberi, or in cases suffering from acute cardiac embarrassment. The preparation of rice polishings is described by Vedder as follows:

"Rice polishings or tiqui-tiqui may be obtained from any rice mill, but should preferably be from a recent milling. The finest grade of polishings should be carefully selected, since some of this product is very coarse and consists mostly of hulls. The tiqui-tiqui is first sifted to remove hulls and weevils. Gauze of about seven meshes to the centimeter is used for this purpose. This fine powder is weighed and mixed with 90 per cent alcohol in the proportion of 3 liters of alcohol to each kg. of polishings. It is then allowed to macerate for twenty-four hours. A glass jar or white enameled receptacle serves for this purpose, and the mixture should be repeatedly stirred or shaken, since the tiqui-tiqui sinks rapidly to the bottom, forming a densely packed mass which the alcohol penetrates with difficulty. During the extraction the alcohol becomes of a deep green color, due to the fat that has been dissolved out. At the end of twenty-four hours the alcohol is siphoned off and filtered until absolutely clear. Since a very considerable quantity remains in the tiqui-tiqui, this should be squeezed in a press, or washed with fresh alcohol, and the residuum filtered and added to the alcoholic filtrate already obtained. The extraction should then be repeated several times, again using 3 liters of alcohol to each kg. of polishings. The combined alcoholic filtrate is then placed in a water bath provided with a thermometer, and an electric fan is so arranged as to throw a strong current of air on the surface of the alcohol. As a result of the heat and the movement of air the alcohol rapidly evaporates. It is essential that the temperature of the extract should not be permitted to rise above 80° C., since extended observation has shown that greater heat is liable to decompose the active neuritis-preventing principle. Whenever the temperature of the extract approaches 80° C., the fire should be extinguished until the temperature drops. This process is continued until all the alcohol is evaporated. The residue is poured into a separating funnel and allowed to stand for about an hour, when it will be observed that the liquid has separated into two layers. The upper and larger portion is of a deep green color and consists of the fat. The lower and smaller layer is brown in color, of syrupy consistency, and contains a number of substances that have been extracted by the alcohol. This

lower layer is carefully drawn off, leaving the fat behind. It varies in amount, but about 25 c.c. usually will be obtained from each kg. of polishings. The brown syrupy fluid so obtained from 1 kg. of polishings is diluted to 60 c.c. with distilled water, whereupon a heavy precipitate is formed. This precipitate consists of substances that were soluble in alcohol, but are insoluble in water. After allowing the mixture to stand for a while, the precipitate settles and the clear fluid is filtered off. This filtrate constitutes the extract as we have used it."

Each 60 c.c. contains the substances that have been extracted by this method from 1 kg. of polishings, and constitutes a day's supply for a patient under treatment with frank beriberi, until the vitamin supply of the tissues can be restored by proper food. More recently the product has been improved in the Bureau of Science at Manila (A. H. Wells). This process is devised for quantity production with a minimum use of alcohol. It has been found in practical work that the product of both methods is active and of great therapeutic value. These extracts have been found equally effective in infantile beriberi, being given in amounts proportional to the body weight. Of course in infantile beriberi it is essential that the nursing mother should be provided with a diet as rich in antineuritic vitamin as possible, beans and unpolished rice being particularly suitable as the basis.

If rice polishings are not immediately obtainable in a particular case, fresh milk with fresh eggs offer some available vitamin and brewers' yeast may be added to furnish rich supplies of the vitamin; these may well serve as the chief nourishment of the acutely ill patient who cannot utilize sufficient barley, peas and beans.

Sometimes, with acute cardiac crisis, venesection may be necessary to relieve the overdistention of the right heart, until relief is afforded by administration of the antineuritic vitamin. Constipation is usually present, and calls for judicious consideration. With wet beriberi the use of saline cathartics together with cardiac stimulation by digitalis have been recommended as adjuvants of the specific vitamin therapy. Edematous accumulations, if of serious character, call for the usual measures. If the heart is involved, rest in bed is essential and, if muscular hyperesthesia and cramps are present, relief may be afforded by bromids. Pressure by bedclothes should be guarded against, both because of the hyperesthesia and the tendency to produce talipes equinus. If cardiac trouble does not prevent, muscular tone should be developed by as much suitable outdoor exercise as desirable, together with massage, passive movements, and active stimulation after the acute stages are over. Strychnin is commonly recommended in the late stages. In general the treatment is dietetic and symptomatic, and the choice of diet is indicated sufficiently by the facts given in the preceding paragraphs.

NUTRITIONAL EDEMA

H. Gideon Wells

For centuries it has been known that famines are often accompanied by "epidemics" of dropsy, and also that extensive edema is a common accompaniment of malnutrition in individuals. According to the conditions under which these epidemics of dropsy have been observed, the names war dropsy, prison dropsy, hunger swelling, famine dropsy, and others have been applied. To the individual cases occurring under other conditions have been applied such names as essential, idiopathic or primary edema, salt edema, alimentary dropsy, anemic dropsy, Mehlnährschaden, or others indicative of the supposed etiology. Modern study of nutrition, together with the vast clinical material provided in the World War, has served to clear up this subject to a large extent.

Among the most important historical records of this dropsical condition in epidemic form are those of the destruction of the French Army before Naples in 1528, dropsy epidemics during the Napoleonic campaigns, in the siege of Paris and in the concentration camps during the Boer war. In the old prisons, dropsy was often the commonest cause of death, and epidemic dropsy has been repeatedly observed during famines in India, China and Russia. During the World War dropsy was first observed in Russian war prisoners in Austria, and in the Polish and Russian population of invaded districts. Later it was observed in many groups of war prisoners and in devastated districts throughout the war zone, especially in Poland and Austria, but to some extent in Germany and Roumania.

The fact that edema is the chief symptom in wet beriberi, and especially in the infantile form of the disease, also that edema often occurs in scurvy, and that it is often accompanied with corneal opacity (keratomalacia) resembling that seen in animals or people who are securing inadequate amounts of the fat soluble vitamin A in their food, led to the suspicion that war dropsy also is a condition due to vitamin deficiency. Experimental studies and clinical observations made during the War, however, seem to have excluded vitamin deficiency and to have agreed in putting the responsibility entirely on definite conditions of nutrition. It was found experimentally by Emma Kohman, Maria B. Maver, and others, that a condition of edema is readily produced in animals by keeping them on a diet which has *all three* of the following characteristics: (1) low total caloric supply, and that chiefly in the form of carbohydrates; (2) very low protein content; (3) abundance of water and inorganic salts. Such conditions are furnished for rats and guinea pigs when the diet is exclusively carrots, and dropsy results despite an abundant supply of all

known vitamins. If the proportion of protein is raised, or the proportion of either carbohydrate or of water is lowered, dropsy will not result even with the same low supply of calories. Addition of still more water or fat soluble vitamins does not prevent or relieve the dropsy.

These experiments conform perfectly to the clinical observations made during the War. Dropsy was observed to occur mostly in people subjected to protracted periods of undernutrition, on a diet low in calories which were chiefly furnished as carbohydrates, extremely low in protein, and the bulk made up with fluids. The typical thin vegetable soup with a small amount of bread was the usual basis of war dropsy. Turnips as the basic element of the diet furnished perfect conditions in many areas. Falta states that persons showing war dropsy had usually been getting from 1,200 to 1,400 calories a day, including only 30 to 50 gm. of protein, derived chiefly from thin vegetable soups. Swiss investigators also found dropsy in men compelled to work on a diet of from 800 to 1,200 calories, containing 15 per cent or more of indigestible cellulose, bread containing 97 per cent of potatoes, very little fat, and at most 50 gm. of protein. Work, cold or infections increase the tendency to dropsy by increasing the need for calories.

Chemical studies showed the tremendous nitrogen depletion of these patients, for when fasting they excreted only from 2 to 3 gm. of nitrogen per day, whereas a normal person excretes from 10 to 12 gm. when fasting. The blood proteins are decreased to from 4 to 6.4 per cent (normal being 6.5 to 8.5 per cent), residual nitrogen is low, and the blood and tissue lipoids are much reduced. It has been thought that this lipoid depletion of the vascular endothelium might account for the dropsy through increasing the permeability of the cells.

These facts also explain the edema of beriberi on a rice diet, for here again we meet with a wet food, poor in protein and furnishing chiefly carbohydrate calories. The Mehlnährschaden (starch dropsy) of Czerny, with its conspicuous edema, is also observed in children fed on such watery carbohydrate diets as barley water or proprietary carbohydrate foods used as gruels. Interesting confirmation is furnished by the fact known to veterinarians that horses and cattle develop dropsy when fed on sugar beet residue and distiller's wash, which contain 95 per cent water and only 0.5 per cent of protein.

Treatment.—This is obvious in view of the above facts. Adequate protein and not too much fluid should always be provided in feeding persons in famine districts or on restricted diet. In prisons, concentration camps and in famine relief, *the common reliance on soups is dangerous.* Soups are warm, comforting, filling, and therefore deceptive, for they drown the starved tissues in salt water without providing the food that is the first need. Stews of the richest possible character should be the basic food supply in such conditions. Since cold and work increase the need

for calories, these should be avoided as much as conditions permit. It is remarkable how much the dropsical famine victims suffer from cold and how quickly they succumb to even slight exposures; a frosty night often kills a large proportion of the dropsical persons in a concentration camp. These unfortunates require the maximum of rest, warmth and concentrated, protein-rich food that can be provided under the existing conditions.

The nutritional dropsy of normal times must be avoided and treated on the same basis. A large proportion of the infantile cases occur in babies given barley water or a similar diet for the relief of some alimentary upset; they do well on it at first, and the parents, being well pleased, fail to bring the infant back to the physician, or disregard his orders to discontinue the limited diet after a certain time. Indeed, the rapid rise in weight and visible plumpness of the dropsical child are often looked upon as most delightful evidences of abounding and improving health. Physicians and nurses must appreciate the possibility of such an occurrence whenever they recommend such limited diets as may produce dropsy, and make sure that the danger is avoided.

EPIDEMIC DROPSY

Samuel T. Darling

This disease appeared to attract attention for the first time in India after a great famine of 1876-1877. At that time great numbers of people were suffering from extreme undernourishment. It occurred altogether among natives of India who generally have to subsist on insufficient amounts of an unbalanced ration. In the Orient, whenever East Indians are exposed to continued losses from some debilitating disease and subsist on small quantities of rice, they suffer very often from severe edema, and anemia, slight fever and diarrhea.

During the War prisoners who were confined in certain German prisons and required to subsist on an extremely low diet of substitutes for food suffered severely from a somewhat similar disease. Anemia, dropsy and slight jaundice were the prominent symptoms.

Greig believes that epidemic dropsy is a deficiency disease and there is little doubt that it is, for it exists in the Orient generally wherever Indian natives peculiarly accustomed to a rice diet are required to maintain themselves on insufficient quantities of that cereal. It has been confused with beriberi but there is no nerve involvement as in that disease.

Symptoms.—Generalized edema is the predominant symptom. This begins with involvement of the subcutaneous tissues and later the body

cavities fill with fluid, there is slight fever and progressive anemia. Sometimes, after severe edema, diarrhea develops and the edema disappears to a great extent. This condition of anasarca and diarrhea may alternate in serious cases until death occurs.

Treatment.—Prevention is by a rational dietary in which the deficiencies of the enforced diet are made up. When natives of India who have lived through a famine or two remove to Fiji where food is more abundant and the struggle for existence not so hard, the contrast between them and their children is very remarkable. Much better nourished tissues are seen in the children. The tissues of the parents, however, never seem to be able to recover from the effects of the starving process. These cases are rather difficult to restore to health. It is important that they be placed on a nourishing well-balanced ration without delay. Rice should probably not be entirely deleted from the dietary because from long-continued use it seems to be peculiarly satisfying to the natives and they prefer it to exotic cereals, but beans and other cereals with a higher nitrogenous content should be added to the rice. Greig recommends the pulses. Milk and chicken can be used, and goats flesh among those whose religious laws preclude the use of beef or other meat.

REFERENCES

Berg, Ragnar. Die Vitamine, S. Herzel, Leipzig, 1922.

Eddy. The Vitamine Manual, Williams & Wilkins, 1921.

Eijkman, C. Eine Beri Beri ähnliche Krankheit der Hühner, Virchow's Arch. f. path. Anat., cxlviii, 523, 1897.

Maver, Maria B. Nutritional Edema and "War Dropsy," Journ. Am. Med. Ass., lxxiv, 934, 1920.

McCollum, E. V. The Newer Knowledge of Nutrition, Macmillan Co., 1922.

Sherman and Smith. The Vitamines, Chemical Catalog Co., 1922.

Vedder, Edward B. Beri Beri, Wm. Wood & Co., 1913.

Walshe. Quart. Journ. Med., xi, 320, 1918.

Wells, A. H. Philippine Journ. Sc., xix, 67, 1921.

CHAPTER VII

SCURVY

H. J. Gerstenberger

General Statement.—Scurvy is a disease caused by the absence from the diet of an amount of the antiscorbutic vitamin (water-soluble C) adequate to meet the needs of the individual human being. It is seen most frequently in artificially fed infants at the end of spring, but it occurs as well in older children and in adults, and extremely rarely in breast-fed infants.

It presents itself in a latent or undeveloped form and in an active or advanced form. The clinical picture of the former is principally characterized in most cases by the development of a general state of malnutrition, while that of the latter is due mainly to advanced pathological changes in the vascular and osseous systems.

The symptoms which in combination are peculiarly characteristic of scurvy, especially in infants, are hemorrhage and bony deformity. The true scorbutic nature of these symptoms in numerous cases is clearly brought out by the improvement established by the administration of foods, or food substances rich in antiscorbutic vitamin, which in the case of hemorrhage and the general state of disturbed nutrition is very prompt and seemingly immediate.

History.—Scurvy as a clinical entity has been recognized for centuries. Its cure was accidentally discovered in the year 1600, when sailors aboard three of four English sailing vessels, leaving England for the East Indies, developed the disease, while the sailors of the fourth vessel who had received lime juice in their diet did not. Although individuals, from time to time, have pointed out the importance of similar experiences, it was not until 1795 that a daily ration of lime juice was ordered to be included in the diets of the sailors aboard English ships.

A great deal of interest has recently been developed in the study of the etiology, pathogenesis and symptomatology of this disease following the classical experimental work of Holst and Froelich in the year 1907. These men demonstrated that scurvy can be produced in the guinea pig by feeding a certain diet and that this disease can then be cured by add-

ing to this diet a food substance such as cabbage juice. They then proceeded to submit different foods, known empirically to cure scurvy, to processes such as heating, drying, acidulating, etc., and were able to show that certain methods either completely or partly destroyed or protected the antiscorbutic property of such food substances. It is now everywhere accepted that etiologically, pathologically and clinically scurvy of the guinea pig is identical with human scurvy, except that the characteristic spongy, bluish red swelling of the gums which is seen so frequently in human scurvy is absent in the scorbutic guinea pig. It is likewise recognized that the guinea pig is even more susceptible to the development of this disease than is the human being, the former requiring approximately one-fifth of the actual amount of orange juice considered necessary to protect the human infant.

SYMPTOMS

The clinical picture of scurvy, as we recognize it to-day, depends upon the severity of the malady in the individual case.

At the present time, it seems advantageous and proper to consider clinical scurvy as appearing in the following forms:

Latent.
Active—acute.
Active—chronic.

Latent Scurvy.—Until recently, general indisposition, fretfulness, loss of appetite, a stationary weight curve, pallor, etc., were not considered to be due to scurvy unless some one of the more characteristic scorbutic symptoms, such as spongy, bleeding gums, swelling of lower end of the femur, hemorrhages into the skin, hematuria, etc., were present at the same time. The French have appreciated, for some time (since 1908), that the most common form of scurvy is a state of malnutrition minus the absolutely pathognomonic clinical signs of this disease. They call these cases "formes frustes" and conclude that they are really scorbutic in nature, because of the repeated clinical experience of rapid improvement after specific antiscorbutic therapy. The recent general experience in the observation of the development of scurvy, especially that of Hess, Abels, L. F. Meyer and Nassau and others, agrees with the French view, namely, that, in reality, the most common type of scurvy is what might be called the undeveloped form, characterized by changed disposition, irritability, hyperesthesia, poor appetite, pallor, anemia, stationary weight curve, hyperexcitable reflexes and at times a rapid pulse and respiratory rate—symptoms which disappear suddenly when an adequate amount of orange juice, tomato juice, or cabbage juice are added to the diet.

To this picture of latent scurvy is added, by Nassau and Singer, the finding of many small pin-point petechial hemorrhages which seem to have a predilection for the face and which according to the authors are easily overlooked unless one is on the lookout for them. They claim to have found the petechial hemorrhages present in 15 out of 30 infants (50 per cent) who later developed scurvy. Likewise they include renal hemorrhages in the picture of latent scurvy. It appeared in 11 out of 30 children who later, within from two to twelve weeks, became clearly scorbutic. A bloody nasal discharge also was noticed in some of the children from four to five weeks before the development of the severe and characteristic symptoms of scurvy.

Whether these petechial hemorrhages and all of the above-mentioned symptoms of the latent stage of scurvy are in each instance to be considered scorbutic in nature because they disappear upon administration of an antiscorbutic has been questioned by Aron, who believes that the anemia and malnutrition are due to an insufficient intake, not only of the water soluble C vitamin, but also, and especially, of the water soluble B (D). That one can be led astray by concluding that every pathological condition that improves after the administration of orange juice is actually scorbutic in origin was experienced by the writer when he recently saw cases of herpetic stomatitis respond quickly to the administration of orange juice. Further study of this occurrence led to the conclusion that it was the water soluble B vitamin in the orange juice and not the water soluble C which was responsible for the improvement in these cases. The future, therefore, may prove that more of the cases that have heretofore been accepted to be real *formes frustes* of scurvy are in reality pathological conditions of another etiology, either alone or in combination with scurvy or other nutritional or metabolic disturbances.

Occasionally an objective diagnostic sign may be utilized to advantage in these cases, namely, the determination of the state of permeability of the vessel walls of the forearm by applying the "Rumpel-Leede" test. The object of this is to submit the vessels of the forearm to an increased pressure and stretching by reducing the venous outflow and still permitting an arterial inflow. This is accomplished by placing a rubber bandage above the elbow in a manner that will produce a decided cyanosis which, in its most satisfactory form in our experience, is accompanied by the appearance of vermillion red spots in the blue cyanotic background. Instead of using a rubber bandage, the ordinary rubber-bag blood-pressure apparatus may be used as suggested by Leede. This author used a relatively low pressure varying from 45 to 60 mm. and allowed it to be applied for a period of from five to twenty minutes. We have found it preferable to use a higher pressure and a shorter interval in conformity with Hess. In our experience, however, the effective pressure more often has been in the neighborhood of 80 to 70 rather than 90 to 80. The cuff is allowed

to remain in this position and at the satisfactory pressure for a period of three minutes, when it is removed and a search made for petechial hemorrhages in the skin of the forearm. In normal infants, especially in those that are well developed, we frequently find present at the elbow and just below a number of petechial spots. Only when petechial hemorrhages extend down to the wrist and are quite numerous can any dependable diagnostic importance be attached to it. However, when such a finding is made in conjunction with the above indefinite picture of malnutrition, it is of positive value in making a diagnosis of scurvy. It must be stated in this connection, however, that the degree of increase in capillary permeability does not always correspond to the severity of the general picture. We have seen severe cases of scurvy showing at times only a mildly positive capillary test on the one hand, and, on the other, less severe cases of scurvy showing a marked presence of petechial spots after the application of the Rumpel-Leede test. There evidently are factors necessary to the development of a positive Rumpel-Leede test other than the simple injury to the vessel wall caused by the scorbutic condition of the infant. One could imagine how a reduction in blood volume might be responsible for a mild or negative "capillary test" even in the presence of a severe vessel wall injury.

Occasionally patients with latent scurvy will still be gaining in weight and will seem to be well. Wiltshire reports that the cases of scorbutic hyperkeratosis that he saw in Serbian soldiers were in some instances the best specimens of physical manhood. It may be, however, that Wiltshire's cases had to do more with an increased need for the water-soluble B (D) vitamin rather than with an inadequate supply of C in the diet.

Active Acute Scurvy.—In this stage there is clinical evidence of marked pathological changes having occurred in the vascular and osseous systems. In some cases the hemorrhagic symptoms control the picture; in others, the osseous; and in still others, the two systems seem to be equally responsible.

The usual clinical picture during this stage of severe scurvy presents a pale or ashen gray, anxious and markedly fretful child lying on its back, objecting to being moved or even touched, with one or both legs flexed and abducted in a froglike position. Often there is swelling present, usually at the lower end of the femur and the upper end of the tibia, due to subperiosteal hemorrhages. At times the swelling is most marked in the middle of the shaft of the femur, when the hemorrhages often are not only subperiosteal but intramuscular as well. An X-ray taken at this time may show nothing more than the swelling that is evident to the naked eye, until antiscorbutic therapy has been instituted, when after a short interval the tumor boundaries become clearly recognizable in the X-ray plate.[1]

[1] The swelling may be so great as to be mistaken for new growth as in cases reported by Rotch.—Editor.

The arms in severe cases occasionally are kept immobile and seem paralyzed, most commonly as a result of a separation of the epiphyses either at the epiphyseal line or just below in the diaphysis. This picture is quite like that of Parrot's luetic pseudoparalysis. The latter condition, however, usually is found in infants less than six months of age and is in nearly all instances accompanied by other characteristic signs of congenital syphilis. In the absence of these, a positive Wassermann test will be of great value in coming to a conclusion regarding the identity of the etiological agent.

Ecchymotic bluish-green yellow areas are found at different locations in the skin and subcutaneous tissue of the face, extremities and trunk. Local injury inflicted by the child itself or by the parents in handling it seems to be the main factor in determining the location of these hemorrhages. Some authors describe the appearance of many small petechial hemorrhages, especially at the hair follicles. It is supposed that these petechiæ are the result of the injury caused by the rubbing of clothing while the individual is active. This condition evidently is common in adults and especially so in those having an abundant growth of body hair. It was a frequent finding in such individuals in prison camps during the War. In the experience of the writer spontaneous petechial hemorrhages such as these are uncommon in infants, although they may have been overlooked, as suggested by Nassau and Singer.

The gums, especially those of the upper incisors, are characteristically swollen, spongy, dark bluish-red in color and bleed readily. The swelling at times is so marked that the greatest part of the incisors is hidden from view. The gums about the lower incisors, canines and molars likewise may become involved. If treatment is not instituted in such cases the teeth become loose and may fall out. Likewise, especially under poor hygienic surroundings, ulcerative processes develop which make the local condition still worse. However, in the light of the recent experience of the writer with the treatment of the various types of stomatitis, the ulcerative lesions at the gums probably are due to the activity of Vincent's organisms which seem to thrive and produce pathological changes when the intake of the water soluble B (D) rather than that of the water soluble C is insufficient.

The spongy, swollen, discolored, bleeding gums about the teeth, when present, are pathognomonic scurvy. This symptom never occurs, however, unless the teeth have erupted or are in the process of coming through. But even though the teeth have erupted the gums may show no abnormality at all or only a slight swelling which is not sufficiently characteristic. In other words, the presence of spongy, bleeding, discolored gums is of great diagnostic significance; the absence of this symptom, however, by no means excludes scurvy in a given case.

Hemorrhages into the mucous membrane of the eye, nose and intes-

tine are not uncommon and in the latter locations simulate diphtheria and dysentery.

Hematuria due to hemorrhages into the kidneys is a common symptom and sometimes the first recognized by the mother. Whenever it occurs scurvy must be considered as an etiological possibility.

In the severe cases hemorrhages may be found almost anywhere. They have been described as occurring in the various organs of the body and especially the different parts of the central nervous system. Cerebral hemorrhages, hemorrhages into the spinal cord and hemorrhages into the sciatic nerve are mentioned. The writer saw 1 case of hemiplegia due to scurvy in a colored girl of eight years, followed by recovery. A unilateral exophthalmous due to hemorrhages beneath the orbital periosteum has been reported by various men. Even deafness has recently been observed as a result of scurvy.[2]

The bleeding time has been found to be normal, the coagulation time in some cases is slightly increased, the platelet count rather increased than decreased, the white count varying within normal limits and usually presenting in the differential picture a preponderance of lymphocytes. The observations by different authors regarding the red count and the hemoglobin determination vary decidedly, showing in some cases a decrease in the number of red cells and in others a very marked increase above normal. Similarly, divergent hemoglobin percentages have been found making it impossible, according to Salle and Rosenberg, to classify the blood picture under any of the anemias. Sometimes a chlorotic blood picture is present. It seems to the writer possible that, in addition to the development of a secondary anemia, the prolonged reduced intake of pigments may be a factor in determining the degree of pallor in some cases.

Oliguresis is a rather frequent symptom of scurvy. This is replaced by a marked increase in water output by the kidney when antiscorbutic therapy becomes effective. In the opinion of the writer this is a specific effect of the antiscorbutic agent and is not, as Hess thinks, due to the plain diuretic property of orange juice. It is not known whether the oliguresis is due to an abnormal retention of water by some patients during certain stages of scurvy in the form of a visible edema which, according to Hess, does not pit on pressure, or to the development of an invisible edema in the sense of Wallgren as a result of a disturbance in the water balance of the body cells, or to a protective salt retention or hindered salt excretion with coincident increase in the water output by the lungs, as suggested by the writer.

The symptoms in the osseous system, which are not necessarily accompanied by hemorrhages, that occur so frequently under the periosteum of the bones of the extremities and of the skull, are a change in the normal

[2] In adults hemorrhages into the muscles forming localized tumors are common. —Editor.

conformation in the first place of the costochondral junctions and, in the second place, of the epiphyses, especially at the wrist.

Clinically these two lesions very often cannot be differentiated from similar deformities produced by rickets. As a matter of fact, the greatest percentage of infants showing these symptoms of the osseous system are suffering both from rickets and scurvy. We can be sure of this in the light of recent confirmatory addition to our knowledge regarding the great frequency of rickets, especially in artificially fed infants, at the end of winter and spring, at a time when scurvy likewise seems to occur in greater frequency. The reason for the increased frequency of rickets at this time of the year in our climate is now recognized as being due mainly to a prolonged absence of sunlight, a factor which plays no direct rôle in the development of scurvy. And yet it is most probable that the absence of sunlight does after all influence the development and incidence of scurvy in artificially fed infants in an indirect manner by stopping pasture feeding and by so increasingly reducing the antiscorbutic content of cow's milk as winter goes on and spring comes. That these symptoms, however, do occur without the aid of rickets, solely on the basis of scurvy, is certain. The writer has had occasion to see scurvy develop in infants who were fed a food that is effectively antirachitic. In these cases the X-ray pictures of the bones are different than they are in cases of scurvy and rickets together or rickets alone. Only under such circumstances is it possible to obtain X-ray pictures typically characteristic of scurvy (see Figs. 1 and 2, pages 78 and 79).

While clinically the widening of the epiphyses at the wrist cannot be differentiated from the same pathological condition produced by rickets, the change in the contour of the costochondral junctions can, in a large per cent of cases of scurvy uncomplicated by the presence of rickets, be recognized as scorbutic from the shape of the deformity produced. The term that, in the opinion of the writer, best fits the scorbutic rosary is the one of "autopsy chest." This is produced by an abrupt dropping down, beneath the level of the ribs, of the sternum and the costal cartilages in toto, either alone or in conjunction with the adjoining rib ends. In some cases the drop is distinctly at right angles just as we see it on the postmortem table when the sternum and the costal cartilages are replaced in the cadaver. This type of deformity is due to the changes in the scorbutic bone that facilitate either the production of infractions at the proximal end of the ribs or epiphyseal separations. Occasionally a similar deformity will be found in rachitic children who show no dependable signs of scurvy.

Non-specific symptoms which occur during the active stage of scurvy are pallor, fever, sleeplessness and loss of appetite. The fever is usually present in a mild degree, oscillating slightly above or below 38° C. Occasionally the temperature reaches higher levels. What part secondary infections play in this it is difficult to say. That intercurrent infections

are not always responsible for the high fever seems clear from the fact that usually there is a relative lymphocytosis. Yet it may be that in most instances the fever is due to the presence of microörganisms whose activity is stopped because the administration of an antiscorbutic substance has made the soil unsuitable to their existence.

Abels is of the opinion that not only the fever but all of the severe hemorrhagic symptoms of the active stage of scurvy as well are due to bacterial action as a result of the state of dysergia present in the scorbutic organisms. It hardly seems justified to the writer to be quite so inclusive as Abels is when one considers the ineffectiveness of the antiscorbutic therapy in conditions that clinically are much like scurvy and without question due to the activity of pathogenic organisms. Cases of sepsis, especially as they occur in breast-fed infants at the age of from eight to twelve weeks, are good illustrations. They look strikingly like cases of scurvy and present many of the symptoms, such as fever, pallor, secondary anemia, loss of appetite, stationary weight curve, fretfulness, tenderness to pressure to the long bones, petechial and ecchymotic hemorrhages into the skin, mucous membranes, kidneys, etc. Spongy gums and the characteristic scorbutic changes in the bones are the only symptoms of real scurvy that cannot be found in these cases. Pogorschelsky reports such a case which in addition showed fractures in the long bones. He suggests that the fractures were the result of an insufficiency of the fat-soluble A vitamin or of the lipoids in the milk of the mother.

Changes in the skin and its appendages, other than those of a decidedly hemorrhagic character described as being due to scurvy, are eczema, hyperkeratosis and a thinning and drying of the hair. These conditions have been considered scorbutic in nature because of their rapid disappearance after the administration of an antiscorbutic. They may be associated, however, more with a disturbance of the water-soluble B (D) metabolism than with an insufficiency of the antiscorbutic vitamin.

Active Chronic Scurvy.—This stage presents the same symptoms as those mentioned under the active acute stage, except that they are not so marked, and develop slowly and come and go. It is an active stage that is alternatingly lessened and increased in degree by an irregular and insufficient intake of antiscorbutic material or by a varying presence of the predisposing and augmenting causes, such as age, time of year and infections. In its mildest form it is represented by the symptoms mentioned under the latent stage with the addition of signs that are specifically suggestive of scurvy, such as black and blue spots in the skin, tender femurs and injected gums.

In its more marked form it presents symptoms that are pathognomonic of scurvy, such as spongy, bluish-red gums, hematuria, subperiosteal hemorrhage. The general condition of the child, however, does not make the serious impression we get in the active acute form. During the spring

of 1923 the writer had occasion to see such a child whose history well illustrates this stage. The gums of this patient were tremendously swollen, dark blue-red in color and bled easily. They completely covered the teeth and a swollen mass extended back from the upper incisors for a distance of a centimeter. A slight fever was present, the child was pale but had a contented look and showed only slight pain to pressure applied at the lower end of the femur. The capillary permeability was only slightly below normal and the urine was negative. An "autopsy chest" rosary and an enlargement of the epiphyses at the wrist were present. These were not rachitic as the diet of the child was adequately antirachitic in nature. The X-ray plate of the wrist showed a non-rachitic bone with a typical scorbutic Fränkel line and destruction of bone beneath with separation at places. Upon the administration of an antiscorbutic food in a sterilized form there was a rapid clinical improvement as was clearly objectively evident from the quick disappearance of the spongy gums. In this case the history showed that the mother had been advised of the need of continuing to give her one-year-old son a definite amount of orange juice and green vegetables. Partly as a result of a varying appetite and partly because of an underestimation by the mother of the importance of the advice given her by the physician, the patient's intake of antiscorbutic substance varied and as a result an oscillating condition of poor and better health began to develop and to exist over a relatively long period, ending finally in the picture described above, which finally had stimulated the mother to consult her physician again. Had the parent over a short period ceased entirely to give antiscorbutic food to this patient, a much more serious general state of debility and severe specific symptoms of scurvy would have followed in an explosive fashion, such as was the experience of Chick and her co-workers in Vienna.

ETIOLOGY

Scurvy is a classical example of what to-day generally are called deficiency diseases, namely, pathological conditions brought on by the complete absence from or the insufficient presence in the diet of a specific, essential food constituent, and prevented and cured by the sole addition of this agent in sufficient quantity to the diet.

The antiscorbutic vitamin or water-soluble C growth factor, as it is also called, is the specific factor concerned in the production, prevention and cure of scurvy.

The original idea that bacteria infection and toxemia were the primary factors in the development of scurvy has been dropped. Recently, however, some authors (Hess, Stolte, Abels, L. F. Meyer) are giving to bacteria a prominent rôle in developing certain symptoms such as fever,

on the one hand, and in increasing the severity of the scurvy and bringing it out of the latent into the active stage on the other.

According to this idea the absence of an adequate amount of the water-soluble C vitamin from the diet produces at first a state of dystrophia and then one of dysergia during which resistance and immunity are lowered and as a consequence of which bacterial activity is enhanced. As a result two things happen: (1) the bacterial injury to the vessel wall is added to the angiotrophic lesions produced by the insufficiency of the vitamin C in the diet; and (2) the bacterial activity drains upon the vitamin store, produces a vicious circle and makes more severe the true scorbutic lesions.

Under such circumstances it is difficult, if not impossible, to evaluate the rôle played by the one or the other (Hess). The writer has suggested a similar explanation in connection with the development of aphthous and ulcerative stomatitis, which complicate certain cases of pure herpetic stomatitis, a condition which seems to be due to a metabolic disturbance associated with an increased need of the water soluble B vitamin by the body.

On the basis of the changes produced in the tissues of the mouth as a result of this water soluble B metabolic disturbance, Vincent's organisms, which are constantly present in the mouth in small numbers, find excellent conditions for growth and produce pathological changes, such as ulcerative stomatitis, Vincent's angina and possibly noma.

The attempt of Abels, however, to blame the action of the local mouth bacteria for the typical, swollen, spongy, bluish-red, scorbutic gums seems to the writer not justified.

In the first place the general appearance of the lesion is not that of an inflammatory process due to local bacterial action. Its color is more of a blue than of a red or of a fiery bright red, as is seen so commonly in cases of ulcerative stomatitis due to the activity of Vincent's organisms. And in the second place the outer surface, at least until oozing begins, is intact, suggesting at least that the injurious agent is operating from within. Finally the practically constant earlier and more severe appearance of the gum changes at the upper rather than at the lower central incisors speaks strongly against local external bacterial action as being responsible for the swollen bluish-red spongy gums of scurvy. Bacteria naturally would and do have better facilities for work in the dependent parts of the mouth, that is, in the neighborhood of the lower incisors. And it is true that pyorrhea is much more common in the teeth of the lower jaw than of the upper.

Later on, especially if decayed teeth are present and favorable conditions for the development of Vincents' organisms exist, ulcerations may be produced at the gums as the result of bacterial action.

L. F. Meyer suggests the practicability of accepting Fisher's general classification of etiological factors in scurvy, which is as follows:

1. Necessary, but unessential factors (age and constitution).

2. Essential but not specific factors (infections).
3. Specific factors (inadequate supply of the water-soluble C vitamin).

The term deficiency disease, as it is applied to-day, in the opinion of the writer, is illogically narrow, because its application is limited to the pathological conditions developing as a result of the presence of an insufficient quantity in the diet of one of the at present recognized four vitamins, namely, the fat-soluble A growth factor or the antixenophthalmic vitamin, the water-soluble B (D) growth factor or antiberiberi vitamin, the water-soluble C growth factor or antiscorbutic vitamin and the fat-soluble D growth factor or antirachitic vitamin. It is well known that pathological nutritional states are developed as the result of an insufficient intake of certain proteins or minerals and it is evident that if all or practically all of the protein, or carbohydrate or fat or calcium or potassium, etc., were eliminated from the diet, that normal growth and development would be impossible on the one hand, and possible on the other hand, if the missing food element were included in the diet. In other words, nutritional disturbances brought on in such a manner really are just as much deficiency diseases as those due to the absence from the diet of a sufficient amount of one of the accepted vitamins.

The antiscorbutic vitamin cannot be synthesized by the human, the cow or the guinea pig. Inasmuch as hitherto it has been impossible to produce scurvy in the rat, it must be admitted provisionally that it may be possible for some animals to synthesize this vitamin. Peculiar storage abilities in such animals, however, may be the real explanation.

For the human being it is a settled fact that he must depend upon his food materials to supply him with an adequate amount of this vitamin. And if this food is cow's milk, its content of antiscorbutic substance will depend upon the amount present in the diet of the cow. It has been shown that pasture-fed cows produce milk richer in antiscorbutic vitamin than do cows fed on a so-called dry diet such as is fed during the winter and early spring months. In other words, the antiscorbutic content of milk varies with the diet of the cow; and the food of the cow, generally and practically speaking, contains more of the antiscorbutic vitamin during the summer than it does during the winter. One cannot speak, therefore, of a definite antiscorbutic value of cow's milk, for this depends entirely upon the diet of the cow and this again upon the time of the year, the kind of soil and seed and the intelligence and interest of the owner of the cows.

It seems clear that it will be difficult, if not impossible, to depend upon cows' milk even in its raw state as a source for an adequate supply of the antiscorbutic vitamin. This is no serious situation, because there are available various other foods that are much richer in the antiscorbutic vitamin and some of which are at the same time relatively inexpensive. The canned tomato or the juice expressed from it is the best example

of an economic food of high antiscorbutic value. Tomato juice in addition is very rich in the water-soluble B growth factor and also contains a liberal amount of the fat-soluble A growth factor. It retains its antiscorbutic value even though it has been canned and sterilized and seems to keep it for an indefinite period of years. The most important factor enabling it to do this is its acid reaction. It has been shown that only a slight degree of alkalinity, such as 0.1 to 0.05 normal sodium hydrate, continued for twenty-four hours or even less, will suffice to reduce greatly or entirely destroy the antiscorbutic vitamin, whether it be in orange juice, tomato juice or in any other food.

The potato is another economic food that is fairly rich in this vitamin. No food has been found that is richer than orange juice. The only difficulty in using it continuously is its expense, although progress in developing methods for preserving it in various forms may do much in the near future to make it economically available at all times.

The table on page 71, taken from Hess, gives the approximate relative value of the antiscorbutic power of various foods.

Heat.—Heating in its various forms has long been held principally responsible for the development of scurvy in artificially fed infants because of the empirical knowledge on the one hand that most infants showing scorbutic symptoms have been on a diet of pasteurized milk, condensed milk, boiled milk and dry patent foods and because, on the other hand, a cure, or at least an improvement of the scorbutic patient could be brought about by the feeding of raw cow's milk. It was the general impression that the greater the degree of heat used the more efficacious was the destruction of the antiscorbutic vitamin. However, individual observers, particularly the French writers, Budin and Variot, have maintained that, although they were accustomed to feeding sterilized milk to a great number of infants, they did not meet with cases of scurvy. These experiences have always been to the minds of others a dubious and unexplainable finding, and yet recent developments have substantiated the findings of men like Budin and Variot. It is now known that boiling and sterilizing are not nearly so destructive to the antiscorbutic vitamin as is pasteurization in the form it is generally practiced at the present time. Nobel, in Vienna, recently saw an accidental cure of a number of scorbutic children through the feeding of cow's milk that had been concentrated down to one-half its volume, by boiling from thirty-five to sixty minutes. Evidently by feeding these children milk in such a concentrated form a greater intake of vitamin was brought about. However, it is also clear that boiling could not have had a very deleterious effect upon the antiscorbutic vitamin contained in the milk. The writer had a similar experience when marked cases of scurvy, the first accidentally and the remainder intentionally, were cured by the feeding of Keller's malt soup, a food which has the reputation of being particu-

RELATIVE DISTRIBUTION OF THE ANTISCORBUTIC FACTOR IN THE COMMONER FOODSTUFFS *

Classes of Foodstuffs	*Antiscorbutic Factor*
Meats, Fish, Etc.	
Lean meat (beef, mutton, etc.)	+
Liver	+
Tinned meats	0
Beef juice	+
Milk, Cheese, Etc.	
Milk, cow's, whole raw	+
Milk, cow's, skim raw	+
Milk, cow's, dried	+
Milk, cow's, boiled	Less than +
Milk, cow's, pasteurized	Less than +
Milk, cow's, condensed (sweetened)	Less than +
Eggs	
Fresh	?0
Dried	?0
Cereals, Pulses, Etc.	
Wheat, maize, rice, whole grain	0
Wheat germ	0
Wheat, maize, bran	0
White wheaten flour, pure corn flour, polished rice, etc.	0
Linseed, millet	0
Dried peas, lentils, etc.	0
Soy beans, haricot beans	0
Germinated pulses or cereals	++
Vegetables and Fruits	
Cabbage, fresh	+++
Cabbage, cooked	+
Cabbage, dried	Very slight
Swede, raw expressed juice	++
Lettuce	++
Carrots, fresh raw	+
Carrots, dried	0
Beetroot, raw, expressed juice	Less than +
Potatoes, raw	++
Potato juice, raw	++
Potatoes, cooked	+
Potatoes, dried	0
Beans, fresh, raw	++
Runner beans, pods	+++
Onions	++
Lemon juice, fresh	+++
Lemon juice, preserved	++
Lime juice, fresh	++
Lime juice, preserved	Very slight
Orange juice	+++
Raspberries	++
Grapes	+
Apples	+
Bananas	Very slight
Tomatoes (canned)	++
Turnip, juice (Swede)	++
Turnip, cooked	+
Miscellaneous	
Yeast, autolyzed	0
Meat extract	0
Beer	0
Cod-liver oil	0
Olive oil	0
Human blood	+

* From Hess, A. F., Scurvy, Past and Present. J. B. Lippincott, 1920.

larly efficient in producing scurvy and one which contains in every quart only one-third of a quart of milk. All of the Keller's soup

was boiled in its preparation, made up at one time in lots of thirty quarts and in one instance sterilized in addition under pressure. In other words, boiling, sterilization and an age of from two to four weeks together did not suffice to reduce effectively the antiscorbutic power of this mixture. The malt soup extract used in making the Keller's soup was one and the same for all patients, while the milk was not. No similar result has been obtainable since with other lots of malt soup extract.

Various authors have argued that it is not so much the degree of heat as it is the length of time during which the heat is permitted to act. However, it is now clear that it is not so much the degree of heat nor the length of time during which it is allowed to act, as it is other factors, enhanced by heating, time, and age in their destructive power against antiscorbutic vitamin.

Alkalinity and Oxidation.—At present there are two agents whose identity and ability to destroy the antiscorbutic vitamin are clearly established, namely, alkalinization and oxidation. In the opinion of the writer, heat and age, as at present operating in preserving food materials by canning, cannot have a deleterious effect, if alkalinization and oxidation of the food to be preserved are made impossible.

Harden and Zilva have shown that even so slight an alkaline reaction as 1/50 normal sodium hydrate can destroy the antiscorbutic value of lemon juice if this degree of alkalinity is allowed to continue at room temperature for a number of hours. Another proof of this is the experience that the acid tomatoes withstand sterilization and an age of years without losing to any extent their antiscorbutic power.

Dutcher has demonstrated that the antiscorbutic power of milk can be maintained during pasteurization if carried out in closed vessels. He found further that oxygen bubbled in milk would destroy the antiscorbutic vitamin, whereas carbon dioxid would not. Hydrogen peroxid had the same effect as oxygen. The method of pasteurization employed in modern dairies calls for constant agitation of the milk, as a result of which a new surface of milk is constantly being exposed to air. This method markedly increases the opportunities for exposing all of the milk repeatedly to oxidation. No such opportunity for oxidation occurs during the ordinary boiling of milk and still less during the process of sterilization in sealed vessels and under pressure.

The writer recently had the opportunity of feeding to scorbutic infants, with complete therapeutic results, a food which ordinarily is very effective in producing scurvy, to which in this lot, however, an antiscorbutic had been added before sterilization for fifteen minutes at 240° F. This particular batch was six months old when it cured the scurvy. In other words, sterilization and age in themselves actually are negligible factors in destroying the antiscorbutic vitamin, whereas alkaline reaction and oxidation are not.

From a practical standpoint, however, heat and age do play a part in aiding the development of scurvy, because in the average home the appreciation of what alkaline reaction and oxidation really mean will be inadequate and also because of the fact that the antiscorbutic value of food and food materials varies and may be very small at times. For instance, vegetables such as potatoes and carrots lose quite a bit of their antiscorbutic value as they, in their natural state, grow older and tougher during winter and spring storage. So it is clear that all factors enhancing the destruction of the antiscorbutic vitamin, even though they be of relatively minor importance, may be the determining factors in making the intake of the antiscorbutic vitamin insufficient and should be eliminated as far as it is possible to do so.

Drying.—Drying in itself need not materially reduce the antiscorbutic value of foods, if it is carried out under conditions that eliminate or lessen oxidation. It is known that milk dried by being blown into an atmosphere of CO_2 is but little harmed as compared with milk sprayed into ordinary air. Likewise milk dried over heated rollers has but little chance for oxidation and consequently does not lose much of its antiscorbutic power. Milk dried by the latter process is not completely soluble and consequently suffers in a practical way from this handicap.

While the drying process bears a similar relationship in its destructive power to the antiscorbutic vitamin as does sterilization, it is practically more often a factor in actually lessening to a greater degree the antiscorbutic value of a food, because it is more difficult to eliminate the factor of oxidation in a practical and economical manner. Possibly the addition of a marked excess of antiscorbutic material to a food to be dried might still leave enough of the active vitamin in the food to make it safely antiscorbutic.

Recently an encouraging report has been made by Cavanaugh, Dutcher and Hall, according to which they have been able to spray milk into the air without losing its antiscorbutic value to the guinea pig, if it was fed not later than twenty-four hours after it had been dried.

Type of Diet.—It has long been recognized that proprietary foods more often than any other food or milk mixture are responsible for the development of scurvy. Practically all of these foods are characterized by a high carbohydrate and low milk content, and some in addition have been alkalinized. All such foods have been subjected to heat and most of them to drying in addition. Whether the high relative carbohydrate intake that is established when these foods are used requires a correspondingly high intake of the antiscorbutic vitamin or not is a question. In all probability the other characteristics of these foods, especially their low milk content, their having been dried and especially alkalinized, are responsible for their scurvy-producing power. It is possible, however, that any high caloric diet of whatever make-up which is causing a rela-

tively rapid increase in weight may require a correspondingly high increase in antiscorbutic vitamin intake and in the absence of such an increase or in the presence of a marked reduction in the antiscorbutic vitamin intake will produce a severe scurvy more readily than a low caloric diet. This seems to apply to rickets also. Chick and her co-workers recently, as a result of a study of an explosive outbreak of scurvy in a group of Vienna children, have come to the conclusion that a diet producing a marked metabolic activity and growth will favor the rapid development of scurvy when the vitamin intake is low. Stefanson maintains that salt is a factor in destroying the antiscorbutic vitamin, and Faber saw a case of scurvy develop on raw milk to which had been added sodium citrate and raises the question as to whether the salt had not been the destructive agent. The liberal use of salt in the making of sauerkraut may be the explanation for its reported lack of antiscorbutic value. The writer, however, found that a batch of sauerkraut made in his own home during the fall of 1922 was antiscorbutic for guinea pigs at the end of the spring of 1923.

Heredity.—Some infants seem more disposed to the development of scurvy than others. This difference has been observed in institutions and camps where frequently the diet has been practically the same for all persons of a given age. The best illustration of the existence of a hereditary factor is the fact that scurvy has been reported as being developed in one of twins even though both were taking the same food. This same difference can be noted in guinea pigs, both as regards the time interval required to develop the disease and also as to the kind and degree of lesions produced in the individual pigs. The writer a few years ago had occasion to observe an exceptionally rare guinea pig who continued to remain well and free from scurvy for a period of three months, even though the diet consisted only of oats, water and hay, which mixture was responsible at the same time for the development of typical scurvy in other guinea pigs at the end of approximately three weeks.

PATHOGENESIS

It is not known in what manner the pathological changes in scurvy are produced by the absence from the diet of an adequate amount of the antiscorbutic substance. Various theories have been advanced, but none have been proved as yet. The fact that the antiscorbutic vitamin, for instance, in canned tomatoes, can withstand sterilization under pressure proves that the vitamin cannot be an enzyme. Yet the antiscorbutic substance may operate over enzyme action either by activating or handicapping some essential enzyme. The work of Bessesen, which shows that the adrenals in scorbutic guinea pigs are 277 per cent above normal weight,

while the weight of the body and other organs as a whole is 16.3 per cent below normal, indicates the possibility of a disturbed internal secretion being concerned in the development of the scorbutic picture.

It may be that a proportionate amount of antiscorbutic substance is necessary for the building of new cells and for the operating of those existing. Funk, Braddon and Cooper have suggested that the symptoms of another deficiency disease, namely, beriberi, are produced by a break in the carbohydrate metabolism, due to a disproportion existing in the diet between carbohydrate on the one hand and the water-soluble B growth factor on the other. In 1918 the writer, in applying the same thought to scurvy, suggested that in the case of scurvy as a result of this break in carbohydrate metabolism a substance was produced that had a strong affinity for calcium, possibly oxalic acid. This product, by defunctioning calcium, especially in the bones and vessels, for instance, might produce vessel leakage on the one hand and Fränkel's white line on the other. However, it has been impossible to prove the cause for oxalic acid. This does not, however, exclude the production of some other substance having similar affinities. Aschoff and Koch later in 1919 have offered practically the same explanation by suggesting that the pathology was due to an injury to the entire reticulo-endothelial apparatus (Kupffer's cells, spleen, lymph gland, bone marrow, endothelial vessel cells), causing an interference with the cementing of the vessel walls.

PATHOLOGY

Gross Pathology.—The gross pathology, just as the clinical picture of scurvy, is controlled or influenced everywhere by the appearance of hemorrhages, except in certain parts of the bone where, in addition to signs of hemorrhage, changes in structure, contour and appearance of the bone occur.

There is nothing particularly characteristic about the hemorrhages; they may be found in any organ of the body, including the brain, spinal cord and the nerve sheaths. The most extensive hemorrhages as a rule occur under the periosteum, which as a result is frequently raised from the bone. Another interesting finding seen is the hemorrhagic swelling of the adrenals.

The most distinctive non-hemorrhagic pathological lesions in the bones are the changes in the character of the marrow and in the structure of the long bones at the epiphyseal end of the diaphysis, especially of the ribs, distal ends of the femur, ulna, radius and proximal end of the tibia and fibula.

The marrow is yellowish in color, reduced in amount and degenerated. Just beneath the epiphyseal-diaphyseal line in the diaphysis infractions were often seen accompanied by swelling. Occasionally the epiphysis is found separated from the diaphysis, but more often this separation is

simulated as a result of the increased fragility of the bone in the upper end of the diaphysis.

Howe has studied the teeth of scorbutic guinea pigs and monkeys and has found definite macroscopic changes in the teeth which seem to be identical with human dental caries.

Microscopic Pathology.—Recently the first positive microscopic evidence of a structure change in the vessel walls of scorbutic patients has been offered by Ide. He considers the condition found to be due to a primary involvement of the intima, which is followed by proliferative changes and a destruction of the elastic membrane, causing in this manner a weakening of the vessel wall. He considers these changes to be endarteritic in nature. He found them in medium-sized arteries. Ide is not certain that these changes are characteristic of scurvy. Aschoff and Koch found no microscopic evidence of vessel-wall injury in scurvy and concluded that the pathological changes are due to injury of the entire reticulo-endothelial apparatus, and that as a result the cement substance is affected which in turn is responsible for the hemorrhages and the bone changes.

The most typical changes are seen in the ribs at the junction of the diaphysis and the epiphysis. In contradistinction to rickets there is present, in the case of scurvy uncomplicated with rickets, an increased amount of calcium which in the X-ray plate appears as the so-called Fränkel's white line. Beneath this is a transverse yellowish area of destruction and confusion, the so-called Trümmerfeld zone, in which are found fragmented normal tissue, trabeculæ of bone, evidence of hemorrhage and irregularly arranged cells. The osteoblasts are few in number and this lack of activity by them is supposed to be mainly responsible for the changes as they follow each other.

Zilva and Wells and Robb and his collaborators have found definite histological changes in the pulp and dentine from animals on a diet deficient in the antiscorbutic vitamin and recently Toverud has examined microscopically the teeth of Howe's scorbutic guinea pigs and monkeys and has found similar changes. Toverud also made chemical analyses of these teeth and met with a decided reduction in the ash and calcium content and with an increase in the magnesium percentage. He suggests that the high magnesium content may account for the very brittle condition of the teeth in scorbutic guinea pigs.

DIAGNOSIS

The diagnosis of scurvy in the acute active stage presents no difficulties. The combination of spongy, swollen, bluish-red bleeding gums, together with tender swollen lower ends of the femurs alone, is pathognomic of this condition.

In the latent stage without a decidedly positive Rumpel-Leede test

or the finding of the characteristic X-ray picture (Fränkel's white line) only a presumptive diagnosis can be made. A history of prolonged feeding of a mixture made from pasteurized milk or some other proscorbutic food without the intake of any antiscorbutic food would be strong circumstantial evidence in favor of a diagnosis of scurvy. And if in addition an immediate, rapid, and complete change and improvement in the symptoms followed the addition of a liberal amount of antiscorbutic substance —orange juice, tomato juice—a positive diagnosis of scurvy could be made with a great degree of certainty. One must be cautious, however, in all disease not to use the therapeutic *post hoc ergo propter hoc* argument too freely. Time and again symptoms will disappear just as readily without the use of certain therapeutic measures as with their application. Nevertheless, from a standpoint of the welfare of the patient, a presumptive diagnosis is justified in every case of malnutrition whose feeding history indicates that the diet has been free from or very low in antiscorbutic material for a period of from three to six months.

It is necessary, however, in the light of recent experiences to point out again the possibility of a disturbance in the metabolism of the water-soluble B (D) vitamin as being at the bottom of some of the *formes frustes* of scurvy, especially when the body weight is normal and the general state of health not bad. The liberal administration of the water-soluble B (D) vitamin in the form of some potent brewer's yeast product will make possible the exclusion of the etiologic activity of this factor.

Frequently a sensitive lower femur is considered to be an adequate diagnostic sign of scurvy. From the standpoint of a scientifically correct diagnosis, however, this sign may be very misleading. Often this sensitiveness to pressure can be elicited during the course of infectious diseases, especially during an attack of follicular enteritis or pyelitis. The customary treatment instituted in these conditions often will cause the sensitiveness to disappear without the additional use of an antiscorbutic and so will eliminate scurvy. These infections, however, frequently are present in scorbutic infants and a dual therapy will be necessary to cure the patient.

Osteomyelitis of the femur might easily be mistaken for a scorbutic subperiosteal hemorrhage and vice versa. An X-ray picture, a Rumpel-Leede test, a careful feeding history and a consideration of the age of the patient and the time of the year will aid in making a correct diagnosis. Scorbutic hematomata sometimes proceed to suppuration and under such circumstances a characteristically rapid general and local improvement after specific therapy will be of diagnostic significance. In every case of osteomyelitis occurring in infants, after the age of four months, the possibility of scurvy should be considered seriously and other scorbutic symptoms sought for. Rheumatism should never cause any diagnostic difficulty. Hemorrhage from the nose, intestine and kidney in an infant four

months or more of age always should make scurvy a diagnostic possibility in the mind of the physician. These symptoms, however, should not be considered scorbutic in nature unless additional evidence, such as indicated above, can be obtained. In every case of unilateral exophthalmos, scurvy must be considered as an etiological factor.

A picture which in many respects resembles severe scurvy is not uncommonly seen in infants at the breast, especially during the first and second quarters of the year. It is characterized by fever, pallor, hemor-

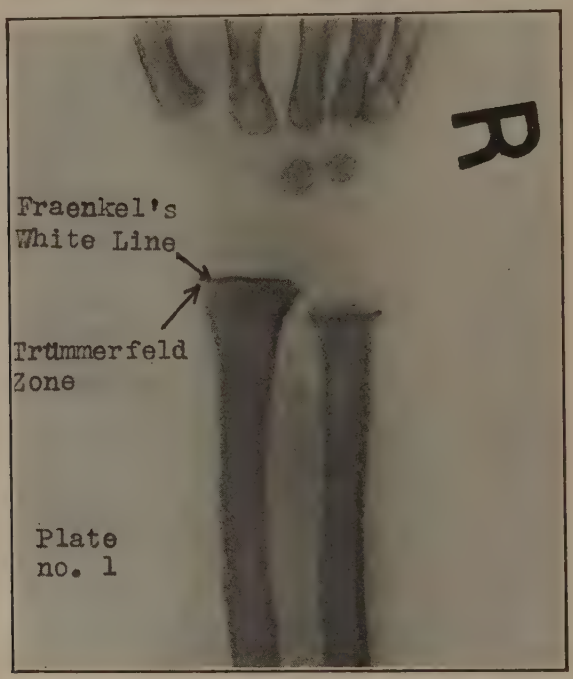


Fig. 1.—X-ray Showing Fraenkel's White Line and the Trümmerfeld Zone

rhages into the skin, subcutaneous tissue and mucous membranes, especially of the nose and intestines. The bones are very sensitive to pressure. That this condition is not due to scurvy is definitely proved by its failure to improve after the administration of liberal quantities of orange juice. Occasionally a positive Wassermann test may uncover the etiological factor. Usually, however, these symptoms are the result of septicemia. The fact that most of these infants are breast fed also speaks decidedly against scurvy. As a matter of fact, scurvy should not be diagnosed as occurring in a breast-fed infant, unless some of the pathognomonic clinical signs are present and a characteristically rapid improvement follows the administration of orange juice.

X-ray.—There seems to be doubt in the minds of certain investigators as to the diagnostic value of the X-ray picture in a case of scurvy. This

applies especially to Fränkel's white line at the junction of the epiphysis and the diaphysis. This difference of opinion is most likely due to the fact that it is not appreciated that nearly every child ill with scurvy is also suffering from rickets and that, therefore, the changes that result in the bone and are presented in the X-ray plate cannot be characteristic

Fig. 2.—X-ray Showing Fraenkel's White Line and the Trümmerfeld Zone

of scurvy for the simple reason that the pathology occurring in rickets is due to the loss of the power of calcification with a resulting overproduction of calcium-free osteoid tissue, while in scurvy the difficulty lies beyond this point, namely, in the breakdown of the osteoblastic function to ossify. Only in a non-rachitic child can a definite, characteristic scorbutic X-ray picture be obtained and this has two characteristics: in the first place, there is an increased deposition of calcium at the junction of the epiphyses and the diaphyses which appears as a widened and em-

phasized white line; and in the second place, a slight distance below the epiphyseal line a zone of destruction develops which in the X-ray plate appears as a hazy area minus the normal amount of calcium. As the fragility increases with the further development of scurvy, an infraction and even a separation may occur which can be recognized in the X-ray plate, especially when a dislocation has taken place at the same time (see Figures 1 and 2 showing Fränkel's white line and the Trümmerfeld Zone beneath). Wimberger calls attention to the presence of seam of shadow about the epiphyseal centers of ossification of the long bones, which he considers characteristic of scurvy.

When an active case of rickets is being treated successfully there is deposited at the epiphyseal line an increased amount of calcium which appears in the X-ray plate in the form of a white line that is exactly similar to one seen in scurvy, except that it usually appears in rickets in a bone that is goblet-shaped. In other words, the white line in itself is not necessarily characteristic of scurvy. It is necessary to consider the rest of the X-ray plate and also the feeding history. In the case of scurvy the white line appears principally during the development of the pathological change, whereas in rickets it is produced during recovery.

PROGNOSIS

The prognosis of scurvy is good, if it is possible to administer an adequate amount of an antiscorbutic food. In most cases, even of the severest type, the improvement in the clinical symptoms is prompt and ultimately complete. The child within from twenty-four to seventy-two hours is comfortable and happy. Months, however, may elapse before the bones return to normal, as seen through the X-ray plate. L. F. Meyer and Stern believe that the same delayed complete recovery applies to the vessels. From personal observations the writer doubts the correctness of this view. Not every crop of petechial hemorrhages that develop after or during a later infection in an infant who has once had scurvy should be considered indicative of the presence of a remaining scorbutic injury.

The prognosis does not depend solely upon the scurvy itself, but also on the degree to which intercurrent infections, such as pneumonia, enteritis, furunculosis, pyelitis, etc., have established themselves. Usually, however, a vigorous antiscorbutic therapy in such cases seems to be of great therapeutic value in fighting the infections themselves.

Leichentritt and Zielaskowski recently found the serum of scorbutic infants low in what are called trypanocidal substances, while Hamburger and Goldschmidt find a normal amboceptor and complement content in the sera of scorbutic infants and animals.

TREATMENT

This resolves itself into getting the patient to take a liberal amount of antiscorbutic food. The best practical antiscorbutic substance is orange juice. One ounce of orange juice four times daily will suffice to produce rapid improvement in the most severe cases of scurvy. There is no objection to offering double the quantity for a few days. The writer has given as high as one pint of orange juice in twenty-four hours without causing any discomfort or diarrhea. It is the general impression that orange juice has distinct laxative properties, and at the present time it is being used mainly for this reason. Many cases of scurvy result from this erroneous idea, because, whenever the stools are soft and are being evacuated daily, the parent stops the giving of orange juice. The only real indication, however, for the giving of orange juice should be to supply the need of the infant of antiscorbutic substance. The writer has had occasion to show that orange juice is more of a diuretic than it is a laxative, and as a result will tend more often towards constipation than towards diarrhea. After improvement has been established as a result of the liberal administration of orange juice, one ounce of this material twice daily will give sufficient antiscorbutic material to any child under all circumstances. The juice of canned tomatoes is the second antiscorbutic food of choice. While it is not quite as potent as orange juice, it is nearly so and the above doses mentioned for orange juice apply to this food substance as well. The great advantage of tomato juice is its availability throughout the entire year and its relatively low cost. Strawberry juice is highly antiscorbutic, as is also lemon juice. The latter may be added directly to the milk after it has been boiled and cooled. Orange juice may be used in the same manner. Occasionally it is difficult to get the parent to give to the child the prescribed amount of antiscorbutic material. This is liable to occur in neurotic families where both parent and child are at fault. A temporary separation of the two by placing the child in a hospital will solve the problem. If necessary tube feeding can be instituted for a few days. Various authors recommend that change of the diet in addition to giving liberal quantities of an antiscorbutic food. This is not necessary, although there is no objection to changing from pasturized milk to boiled milk and from oatmeal water to potato water in addition to giving orange juice or tomato juice.

PREVENTION

Too much emphasis cannot be laid upon the importance and the ease of preventing scurvy, especially in its latent form. From the data presented above it is evident that abnormal nutrition, dental caries and bacterial activity are made possible by scurvy.

The exact amount of an antiscorbutic substance, such as orange juice,

that is necessary to prevent the development of scurvy in any of its forms, is not positively known. Theoretically this amount will depend upon various factors, such as the predisposition of a patient, the kind of food, the amount of food ingested and the rate of metabolism and growth. There exists, in all probability, an ideal proportion between these factors on the one hand and the required amount of antiscorbutic vitamin on the other. From a practical standpoint, however, it is advisable to be liberal in establishing the amount of antiscorbutic material considered necessary for the prevention of scurvy. Therefore, it may be stated that every infant that is bottle fed, not later than one week after it receives artificial food, either alone or together with breast milk, should receive the antiscorbutic substance in the form of orange juice or tomato juice. The age and general condition of the infant, whatever they may be, present no contra-indications. The writer has fed orange juice and tomato juice without harm or difficulty to premature infants and those aged one week. Usually the dose at the beginning has been at least 1 c.c. (¼ teaspoonful) twice daily. This dose has gradually been increased within one month to a total of 15 c.c. (1 tablespoonful) twice daily. Later on, especially when the diet consists of a food that is known to be proscorbutic, as high as 30 c.c. (2 tablespoonfuls) have been administered twice daily. The same doses have been used for the administration of tomato juice, except in older infants when as much as 60 c.c. (4 tablespoonfuls) have been given twice daily.

Whether the orange juice is diluted with boiled water or not is immaterial so long as the ordered amount of antiscorbutic material is ingested. If the orange juice is too sour, it may be sweetened by the addition of a sufficient amount of sodium bicarbonate just before the administration of the juice. It is important to realize that, if orange juice which has been neutralized with baking soda is allowed to stand even for a relatively short time of a few hours, the antiscorbutic property will be markedly reduced.

From the data presented above under Etiology it is clear that boiled milk is preferable to pasteurized milk from the standpoint of protection of the antiscorbutic vitamin. In small communities or in the country where general pasteurization of the milk supply is not required by law, this is the method of choice. Raw milk will contain even more of the antiscorbutic substance than will the same milk after it has been boiled. However, generally speaking, there may be present in raw milk, in the form of pathogenic bacteria, by far greater sources of danger to the infant than sources of protection as a result of its relatively higher content of the antiscorbutic vitamin. And then at best the antiscorbutic power of raw milk is low, variable, and therefore not dependable as an adequate source of this vitamin. Consequently it is necessary always to order in addition some substance rich in the antiscorbutic vitamin.

While boiling and sterilizing are less destructive to the antiscorbutic vitamin than pasteurization, the last-named method in all probability will be retained by municipalities as the method of choice in ridding the milk of pathogenic organisms. It does not change the taste of the milk nor does it influence the formation of the so-called cream line upon which characteristics the public and the dairies both lay so much stress. At the same time pasteurization is effective in destroying the pathogenic bacteria contained in the milk. The near future, by changing the process of pasteurization, may make possible no greater destruction of the antiscorbutic vitamin than is produced by boiling. As stated above in order to be certain of preventing scurvy, it is absolutely essential that an additional supply of the antiscorbutic vitamin be administered regularly and in liberal amounts no matter whether the milk used be raw, boiled, sterilized or pasteurized.

Depending upon the age of the infant the doses will vary, beginning for orange juice with 1 c.c. (½ teaspoonful) twice daily and reaching 15 c.c. (1 tablepoonful) twice daily at the end of the first month. For tomato juice the same doses should be adequate, although for older infants and children this may be increased to double the quantity indicated for orange juice.

When the diet of the infant or child includes vegetables, an additional amount of antiscorbutic substance is automatically ingested. The exact amount of the antiscorbutic vitamin, however, will depend upon the kind of vegetables, the age and the method of preparation. The younger and fresher the vegetable and the shorter the time of exposure, during preparation, to air and alkalization, the greater will be its content of active antiscorbutic vitamin. Potatoes, for instance, require much less time for cooking than do carrots, and therefore are much more dependable as a source of the antiscorbutic vitamin than are boiled carrots. Cabbage in its raw state or as cabbage juice is markedly antiscorbutic. In the form of sauerkraut the reports indicate an entire lack of antiscorbutic power, although the lots used by us at the end of winter, as described above, had a high antiscorbutic value.

It is important to appreciate that the richness of a given food substance in antiscorbutic vitamin is not the only deciding factor as to whether a certain food will supply the antiscorbutic needs of the patient, but the quantity of the food regularly consumed as well. Potatoes, even though they are decidedly poorer in antiscorbutic vitamin than are oranges and tomatoes, are represented in the daily diet of most human beings in this country in liberal amounts and so are and have been more responsible for our protection against scurvy, at least in its recognizable form, than have oranges and tomatoes. It seems possible that many children and adults, however, at times, especially at the end of winter, may be subsisting on an intake of antiscorbutic material that is inadequate, and it

therefore would seem to be good preventive advice to encourage, especially during winter and early spring, the use of canned tomatoes or fresh cabbage in the diet of every child and adult at least three times per week in addition to the regular diet, which commonly includes a daily portion of potato. Still better, of course, is the daily consumption of an orange. The high cost, however, is only too often prohibitory.

REFERENCES

Abels, H. The Rôle of Infections in Scurvy, Wien. klin. Wchnschr., No. 41, 33, Oct., 1920; Abstr. in Journ. Am. Med. Ass., lxxvi, 559, 1921.

——— Die Skorbutische Dysergie, Ztschr. f. Kinderh., xxxvi, 295, 1923.

Anderson, E. V., Dutcher, R. A., et al. The Influence of Heat and Oxidation upon the Nutritive and Antiscorbutic Properties of Cow's Milk, Science, liii, 446, 1921.

Aron, Hans. Alimentare Anaemie und Skorbut, Klin. Wchnschr., Jahrg. 1, 2035-2039, July-Dec., 1922.

Aschoff, L., and Kock, W. Skorbut, Fischer, Jena, 1919.

Bassett-Smith, P. W. Further Experiments on the Preservation of Lemon Juice and Prevention of Scurvy, Lancet, ii, 321, 1921.

Bessensen, D. H. Changes in Organ Weights of the Guinea Pig during Experimental Scurvy, Am. Journ. Physiol., lxiii, 245, 1922-1923.

Brandt, Hedwig. Blutuntersuchungen bei Barlowscher-Krankheit, Arch. f. Kinderh., lxvii, 395, 1919.

Cavanaugh, G. W., Dutcher, R. A., and Hall, J. S. The Effect of the Spray Process of Drying on the Vitamine C Content of Milk, Am. Journ. Dis. Child., xxv, 498-502, 1923.

Chick, H., and Dalyell, E. J. Eine Skorbut Epidemie unter Kindren im Alter von 6 bis 14 Jahren, Ztschr. f. Kinderh., Orig., xxvi, 268, 1920.

Delf, E. M. Studies in Experimental Scurvy, Lancet, i, 576, 1922.

——— The Antiscorbutic Value of Cabbage, Biochem. Journ., xii, 416, 1918.

Ellis, N. R., et al. Some Observations on the Stability of the Antiscorbutic Vitamin and Its Behavior to Various Treatments, Journ. Biol. Chem., xlvi, 369, 1921.

Emmet, A. D., and Luros, G. O. Water-soluble Vitamines. I. Are the Antineuritic and the Growth Promoting Water-Soluble B Vitamines, Ibid., xliii, 278, 1920.

Faber, H. K. Infantile Scurvy Following the Use of Raw Certified Milk, Am. Journ. Dis. Child., xxi, 403, 1921.

Frank, H. M. Röntgenologische Nachuntersuchungen bei klinisch. geheilter Möller-Barlowscher Krankheit, Ztschr. f. Kinderh., Orig., xxvii, 134, 1921.

Gerstenberger, H. J. Malt Soup Extract as an Antiscorbutic, Am. Journ. Dis. Child., xxi, 315, 1921.

——— Pathogenesis of Infantile Scurvy, An Hypothesis, Am. Journ. Med. Sc., clv, 253, 1918.

——— The Etiology and Treatment of Herpetic Stomatitis and Herpes Labialis, Am. Journ. Dis. Child., xxvi, 309-328, 1923.

Gerstenberger, H. J., and Champion, W. M. The Constipating Qualities of Orange Juice, Am. Journ. Dis. Child., xvii, 88, 1919.

Givens, M. H., and McClugage, H. B. The Antiscorbutic Property of Fruits. I. An Experimental Study of Dried Orange Juice, Ibid., xvii, 35, 1919.

——— Antiscorbutic Property of Vegetables. II. Journ. Biol. Chem., xlii, 495, 1920.

Givens, M. H., et al. The Antiscorbutic Properties of Fruits, Am. Journ. Dis. Child., xxiii, 216, 1922.

Gottschalk, Charlotte. Ueber Blutuntersuchungen beim kindlichen Skorbut, Arch. f. Kinderh., lxxiii, 244, 1923.

Hamburger, R., and Goldschmidt, L. Resistenz and Skorbut, Jahrb. f. Kinderh., c, 210, 1922.

Hart, E. B., Steenbock, H., and Smith, D. W. Studies of Experimental Scurvy. Effects of Heat on the Antiscorbutic Properties of Some Milk Products, Journ. Biol. Chem., xxxviii, 314, 1919.

Hausman, T. The Blood Picture with Scurvy, Ztschr. f. klin. Med., xciii, 346, 1922; Abstr. in Journ. Am. Med. Ass., lxxix, 172, 1922.

Hess, Alfred F. Scurvy—Past and Present, Lippincott, 1920.

Hess, Alfred F., and Unger, L. J. The Scurvy of Guinea Pigs. II. Experiments on the Effect of the Addition of Fruits and Vegetables to the Dietary, Journ. Biol. Chem. xxxv, 496, 1918.

——— The Scurvy of Guinea Pigs. III. The Effect of Age, Heat, and Reaction on Antiscorbutic Foods, Ibid., xxxviii, 296, 1919.

——— Scurvy. VIII. Factors Affecting the Antiscorbutic Value of Foods, Am. Journ. Dis. Child., xvii, 238, 1919.

——— The Deleterious Effect of the Alkalization of Infant's Food, Journ. Am. Med. Ass., lxxiii, 1354, 1919.

——— Scorbutic Beading of Ribs, Am. Journ. Dis. Child., xix, 333, 1920.

Howe, P. R. Decalcification of Teeth and Bones, and Regeneration of Bone through Diet, Journ. Am. Med. Ass., lxxix, 1565, 1922.

Ide, T. Gefässveranderungen bei der Möller-Barlowscher Krankheit, Ztschr. f. Kinderh., xxxii, 165, 1922.

Leede, C. Zur Beurteilung des Rumpel-Leedschen Scharlachphenomens, München. med. Wchnschr., No. 31, 1673, 1911.

Leichtentritt, Br., and Zielaskowski, M. Der Gehalt des kindlichen Serums an trypanozider Subtanz, Jahrb. f. Kinderh., xcviii, 328, 1922.

McClelland, R. S. A Case of Scurvy, Lancet, ii, 608, 1921.

McClendon, J. F., Cole, W. C. C., et al. The Effects of Malt and Malt Extracts on Scurvy and the Alkaline Reserve of the Blood, Journ. Biol. Chem., xl, 257, 1919.

McCollum, E. V., and Parsons, H. T. The Antiscorbutic Requirement of the Prairie Dog., Ibid., xliv, 607, 1920.

McLean, S. A Case Report of Scurvy with a Summary of Fifty Other Cases, Arch. Pediat., xxxv, 477, 1918.

Medes, G., and Smith, E. Effect of Heating the Antiscorbutic Vitamine in the Presence of Invertase, Journ. Biol. Chem., xlviii, 323, 1921.

Meyer, L. F. Die skorbutische Diathese, Monatschr. f. Kinderh., xxv, 454, 1923.

Nassau, E., and Singer, M. J. Zur Kenntniss des Vorstadiums der Barlowschen Krankheit, Jahrb. f. Kinderh., xcviii, 44, 1922.

Noble, Ed. Zur Barlow-Frange, Ztschr. f. Kinderh., xxviii, 369, 1921.

Parsons, H. T. The Antiscorbutic Content of Certain Body Tissues of the Rat. The Persistence of the Antiscorbutic Substance in the Liver of the Rat after Long Intervals on a Scorbutic Diet, Journ. Biol. Chem., xliv, 602, 1920.

Pogorschelsky, Herbert. Zur Frage des Auftretens von Skorbut beim Brustkinde, Ztschr. f. Kinderh., xxxv, 244, 1923.

Salle, V., and Rosenberg, M. II. Uber Skorbut, Ergebn. d. inn. Med. u. Kinderh., xix, 31, 1921.

Sammis, J. F. A Case of Scurvy with Cerebral Hemorrhage, Arch. Pediat., xxxvi, 274, 1919.

Seligmann, A. Ein Fall von Ertaubung bei Möller-Barlowscher Krankheit, Monatschr. f. Kinderh., xviii, 222, 1920.

Steele, H. M. Exophthalmos, Due to Scorbutus, Arch. Pediat., xxxviii, 52, 1921.

Stefansson, V. Observations on Three Cases of Scurvy, Journ. Am. Med. Ass., lxxi, 1715, 1918.

Stern, Ruth. Ueber den Zusammenhang von skorbutem Infekt., Ztschr. f. Kinderh., xxxvi, 32, 1923.

Toverud, G. Influence of Diet on Teeth and Bones, Jour. Biol. Chem., lviii, 583, 1923.

Wallgren, A. Zur Symptomatologie und Pathogenese des Oedema scorbuticum invisible, Ztschr. f. Kinderh., xxxi, 35, 1922.

——— Morbus Barlowii bei einem Zwillingskind, Acta Paediatrica, ii, 376, 1922-1923.

Wiltshire, H. Hyperkeratosis of the Hair Follicles in Scurvy, Lancet, ii, 564, 1919.

Wimberger, M. Zur Diagnose der Sauglingsskorbut, Ztschr. f. Kinderh., xxxvi, 279-285, 1923.

CHAPTER VIII

RICKETS

P. G. Shipley

Rickets is perhaps the most common disease of childhood. It is essentially a chronic metabolic derangement frequently of nutritional origin. It does not usually cause death although Park and Howland have shown that of itself it may prove fatal. The condition is constitutional, and all the organs and tissues are undoubtedly involved to a certain extent, although the most marked lesions and the only ones that are now known to be characteristic of the disease are found in the bones.

Historical.—The earliest reference to symptoms of rickets in children is contained in some palm-leaf manuscripts written in Burma—probably during the first century B. C.—an interesting comment on the commonly accepted belief that the disease does not occur or is uncommon in the tropics. One of these manuscripts, moreover, refers to the now well-known tendency of premature infants to develop deformities. Soranus of Ephesus called attention to deformities of the spine and legs which were frequent among the children of Rome and its environs. Some, said he, sought for the cause in the climate, some in the dissolute life of the mothers, and others in the ignorance of the Roman matrons of his day of the art of raising children. The deformities of which he wrote were probably of rachitic origin, but it was not until the year 1650 that Glisson published his classic work *De Rachitide,* in which the disease, which during the previous thirty years had come to be common in England, was carefully studied. Like the word *nonna* which was used in Italy for lethargic encephalitis, the name rickets had its origin among the *vetulæ provinciales* of Dorset and Somerset and was derived from the Old English verb *"wrikken,"* to bend. The word rachitis comes from the Greek νόσος ραχίτης the spinal disease.

Distribution.—This disease is most widespread in cities, and is in some probably almost universal. The temperate zone is most severely afflicted with rickets, which is not common in the arctic. It is generally stated that rickets does not develop in the children of the tropics. Careful

investigation proves that this is not the case, though the condition is by no means as frequent or severe as in the temperate zone except under certain conditions. The disease has clouded the future and stunted the bodies of thousands of children in the central European empires during and since the Great War.

Seasonal Variation.—Active rickets is much more common in the winter than during the warm months of the year. During the winter and early spring the severity of the disease is at its maximum. Children who are born after the month of July are much more liable to contract rickets in their first year, if they are artificially fed, than are those children who are born in the spring of the year.

Rickets in Animals.—Rickets is never found among wild animals but is common among those born in captivity. Its occurrence was, until very lately, the chief obstacle to the rearing of monkeys and lion cubs in zoos. It affects hogs, sheep, cattle, dogs and poultry. Cats, however, perhaps because of their predatory habits, remain apparently immune.

Congenital Rickets.—It is now generally conceded that congenital rickets does not occur, although theoretically there is no reason why it should not. It is, however, certain that there are occasional cases of rickets in which the beginning of the disease must have been coincident with the beginning of extra-uterine life.

Chondrodystrophia fœtalis, osteogenesis imperfecta, and syphilitic disease of the bone have all been described as congenital rickets in the past.

Acute Rickets.—Acute rickets is a misnomer formerly applied to cases of scurvy in infants.

Late Rickets.—The uncommon occurrence of rickets later in life than the usual age, let us say after the fourth year, is described under this name, or as rachitis tarda. According to Hutchinson and Shah this condition is common among young girls of the better classes in India. These children, having been married, are forced, just after the age of puberty, to live on a poor diet in close confinement in dark quarters which they seldom leave. This confinement is part of the condition known as "purdah." The men and women of the poorer class escape, being forced by poverty to work in the sunlit fields.

PATHOLOGY

The only characteristic lesions in the bodies of rachitic children are found in the bones and blood.

Bone Lesions.—Lime salts are not deposited in the bones during growth and as a result there is a compensatory overproduction of uncalcified matrix. The cortex and the trabeculæ of the spongy bone are sur-

rounded by, or in severe cases entirely composed of, osteoid tissue—in other words, a tissue which is identical in structure with true bone, but which fails to become calcified. It should be emphasized that the presence of this osteoid is not due, except perhaps in small part, to resorption of lime salts from previously calcified bone. At the same time the endochondral growth of bone does not proceed normally. The epiphyseal cartilages do not undergo the preparatory calcification which usually precedes ossification. The cartilage of the epiphysis is irregularly invaded by blood-vessels which sprout in all directions from the vascular tree in the shaft of the bone. The replacement of the cartilage by bone is delayed and consequently unchanged cartilage persists in the epiphyseal region of the shaft. As a result of the above-described processes a more or less wide area known as the rachitic metaphysis is formed between the cartilage and the shaft proper. This area is a jumble of osteoid tissue, giant capillary blood-vessels, reticular tissue and cartilage in various stages of metamorphosis or degeneration. Because of the compensatory overproduction of osteoid tissue, the bones of a child with severe rickets are much thicker than those of a normal child, but, being made of inferior material, are much more pliable and bend with abnormal ease under stress or strain. The process does not go on equally throughout the entire skeleton, although the whole bony structure is involved in severe cases. In general, the areas of most rapid growth, for example, the femora, middle ribs and centers of ossification, are most markedly affected.

By reason of these changes the bones show more or less marked curvatures and deformities. In extreme cases there may be marked thickening of the skull, especially over the frontal and parietal eminences. This with flattening of the softened bones of the calvarium results in the square rachitic head. The fontanels are slow to close. In some children areas of softening and thinning of the cranial bones are found—the so-called craniotabes. Curvatures of the spine, usually kyphotic or lateral, occur. The costochondral junctions become enlarged, and the shaft of the ribs may become so dislocated on the costal cartilages as to form acute angles with them, the apices of which point inward. The deformities of the chest may be so marked as to limit the capacity of the thorax and seriously interfere with complete aëration of the lungs. Pathological curvatures of the bones of both upper and lower extremities occur. The normal contours of the bones may disappear altogether. The humerus, the tibia and fibula, the radius and ulna, and even the femora may be bowed. The epiphyses of the long bones are often greatly enlarged so that the wrist, ankle, and knee joints appear swollen.

The changes of rickets are not, except in the most severe cases, uniform throughout the skeleton. The clavicles and the small bones are appreciably affected only in the most severe cases. Infants are seen in whom detectable involvement is limited almost entirely to the bones of

the skull. This is often to be observed in prematurely born children who have developed rickets. In other cases in contrast to very great deformity of the rest of the skeleton the calvarium remains clinically quite normal. *Spontaneous fractures* are common in severe rickets and occur in response to insignificant trauma. They heal with redundant callus formation, and frequently contribute greatly to the residual deformity.

Blood.—Howland and Kramer have shown that calcium is present to the amount of from 8 to 10 mg. in each 100 c.c. and that there are from 4.5 to 6 mg. of inorganic phosphate in the blood-serum of normal children. In the blood-serum of children with uncomplicated rickets the same authors found that the inorganic phosphorus might be reduced to as low as 1 mg. in each 100 c.c. When the rickets heals the phosphorus in the blood rises gradually to normal. If the rickets is complicated, however, by manifest or latent tetany the serum phosphorus remains approximately at the normal level. The calcium falls from about .10 mg. to as low as 3.5 mg. in each 100 c.c. of serum.

Marrow.—The bone marrow of many children with rickets is replaced to a greater or lesser extent by fibrous tissue and many children, but not by any means all, have a more or less severe grade of secondary anemia.

Muscles.—These are usually small, flabby and underdeveloped.

Other Viscera.—The *ligaments* of the joints are usually relaxed and may be elongated. The *lungs* in severe cases may show the marks of the thoracic deformities and, in the parts which have been compressed by the chest wall, may be unexpanded and airless. A low-grade inflammation of the lower air passages is frequent and a bronchopneumonia is often the cause of death. The *spleen* and *lymph glands* are commonly enlarged but the enlargement is the result of a simple hyperplasia and is not characteristic of the disease. The *intestines* are usually atonic and are distended with gas. There are no other essential anatomical lesions known at present.

Teeth.—Dentition is delayed in children with rickets and is liable to be accompanied by digestive upsets. The teeth, however, are usually good during the activity of the disease. It is only later in childhood that they are prone to severe caries.

SYMPTOMS

Rickets is usually recognized and diagnosed by the deformities of the skeleton which are manifest on physical examination or found in roentgenograms. There are, however, certain symptoms which point to the existence of the disease. Rachitic children perspire profusely especially about the head (head sweats) and they are usually restless and uneasy

in their sleep. Constipation is common and the appetite is frequently capricious or poor. The children are usually irritable or apathetic. They cease to move actively and do not learn to sit upright or to walk. Atony of the musculature of the abdominal wall and of the intestinal musculature, which is at least partially responsible for the constipation of rickets, also results in distention of the abdomen and the formation of the so-called "pot belly." Muscular atony and relaxation of the ligaments and tendons are the causes of abnormal flexibility of the limbs so that overextension is possible (when this condition is seen in the knee it is known as genu recurvatum) and the children often sit or sleep in the most bizarre attitudes and positions. A symptom which occurs early in the course of the disease, if at all, is the so-called rachitic tenderness. When present it is most marked over the muscles at the points of insertion. It may be very acute. This tenderness is occasionally seen in puppies suffering with so-called cage or confinement rickets. Since this disease is not true rickets, it is uncertain whether tenderness in children is due to rickets or to some complicating condition at present unrecognized.

EXPERIMENTAL RICKETS

The concrete knowledge which we now have about the etiology of rickets and about its treatment has been almost entirely a result of the application of the experimental method to the study of the disease. Rickets has been found in animals which have been subjected to all sorts of experimental procedures.

Morpurgo described rickets in rats apparently produced through the agency of an organism which he isolated from the tissues of animals which had spontaneously developed the disease. Matti claimed to have produced rickets by extirpating the thymus from very young puppies. Findlay at one time felt that the results of his work showed that rickets resulted from confinement and bad hygiene. In not one of these experiments, however, was the diet of the animals at all controlled. Most of the investigators who have studied rickets in animals have attempted to reproduce the disease by feeding diets faulty in one or more respects. Since the bones of the skeleton in rickets are deficient in calcium salts, it was most natural to attempt to produce the disease by feeding diets low in calcium, with the idea that rickets might be due to a deficient supply of lime salts in the food. Such an experiment was that of Dibbelt, who fed puppies on horse meat and starch. Attempts to produce rickets in this way were not uniformly successful because at the time when they were carried out much of the knowledge which we now have of the relation of the diet to growth and health was unknown.

The first real advance in the campaign against Rickets was made by

Mellanby in England. His experiments showed conclusively that rickets was a dietary disease. He came to the conclusion that rickets was associated with the absence from the diet of either the fat-soluble A vitamin or some other substance which had an analogous distribution.

In the meantime McCollum and his coworkers had produced rickets experimentally in rats under conditions which made an accurate analysis of the faulty diets possible. Their experimental animals developed changes in their bones identical with those seen in rachitic children. They were able to show that rickets was not the result of a deficient supply of the fat-soluble A vitamin in the diet. They produced the disease in rats in two ways: (1) by feeding diets which were, ceteris paribus, low in phosphorus; and (2) by feeding diets which were, ceteris paribus, low in calcium when an organic substance which is contained in cod-liver oil was supplied in deficient amounts and the animals were kept in ordinary room light. The blood of these animals was carefully studied by Howland and Kramer as regards its content of inorganic phosphorus and calcium and their findings were of the greatest interest. They corresponded exactly to the findings in the blood of children with rickets. The inorganic phosphorus of the serum of animals on low phosphate diets fell as low as 2.5 mm. per 100 c.c. The calcium of the serum remained in normal amounts. This is a duplication of findings in the blood of children with uncomplicated rickets. On the other hand, in animals which had received diets low in calcium the phosphorus of the serum was found at the normal level. The calcium, however, was diminished to from 4.5 to 6 mm. per 100 c.c., as is the calcium in the serum of children whose rickets is complicated with tetany. McCollum and his coworkers found that the animals were able to build well-calcified bones on diets which were low in either calcium or phosphate, provided that the diet was so constructed as to maintain a normal balance between these two ions. Some organic substance in cod-liver oil exerted a protective action when the above-mentioned balance was not maintained in the diet. In other words, when cod-liver oil was added to a diet which would have otherwise caused rickets that disease was prevented from developing. Florid rickets in their animals was cured by cod-liver oil. The antirachitic substance in cod-liver oil is not identical with fat-soluble A. It occurs in shark and burbot and other fish oils, in egg yolk fat, and in certain leaves. Coconut oil is the only vegetable oil tested which contains it, and it is present only in small amounts in butter fat.

The work of Howland and Park proved that cod-liver oil cures rickets in children.

In the meantime Huldschinsky, Howland and Kramer, and also Hess demonstrated that sunlight or the light of the mercury vapor lamp would cure rickets in children. Powers and his coworkers showed that it was equally effective against experimental rickets in rats. The healing pro-

cess is chemically and histologically identical in children and in rats. In short, it has been shown that rickets may be induced experimentally by diets which have a defective salt composition. If, however, children or animals are supplied with sufficient amounts of the antirachitic substance, or are exposed to light of short wave-length, rickets does not occur and they are enabled to build well-calcified bone.

ETIOLOGY OF RICKETS IN CHILDREN

There is no longer any reason for believing that rickets is the result of infection, and there is no good evidence which points to syphilis, overfeeding or to a disturbance of the function of the endocrine glands as a cause of the disease.

The work which has been done with animals together with the recent studies on the chemical changes in the blood of rachitic children explain the mechanism which produces rickets. Little light, however, has been thrown on the etiology of rickets in children.

The majority of those who have studied rickets believe it to be the result of faulty nutrition. It is obvious that poor food and faulty hygiene play a prominent part in its development. It is not possible to say at present whether heredity has anything to do with the disease or not. It has seemed as though food which was deficient in fat but contained a superabundance of carbohydrate was most likely to permit rickets to develop.

The problem of the etiology of rickets in children is extraordinarily involved. The number of factors which may be related to the development of rickets is already greater than those which are related to any other known disease. It is not by any means impossible that further study may show that other still unappreciated substances or conditions militate for or against the appearance of rickets.

One of the earliest hypotheses, that is, that rickets was the result of a deficient supply of lime salts to the bones, was exploded by the work of Howland and Marriott when they showed that the blood of rachitic children is normal or nearly normal, as regards its content of calcium. Their work showed that rickets is the result not of insufficient supply of calcium, but of the failure on the part of the child to utilize an abundant supply. Although the blood of children with uncomplicated rickets contains a subnormal amount of phosphorus, by far the greatest number of them are given an abundant supply of this substance in their diet. It is doubtful if the composition of the diet itself, as it is fed, is directly the cause of rickets. It may be said, furthermore, children rarely if ever receive diets which are analogous in composition to those which have been used to induce rickets in animals. Some children develop the disease on the same

diet which will permit normal growth in others. By far the greatest number of rickety children are artificially fed, but a certain number of cases occur in breast-fed infants, especially in those who are for too long a time entirely dependent on maternal nursing. Premature infants are almost certain to be attacked by the disease under the best of conditions and certain other children seem to acquire rickets no matter how they may be fed. Some of the difference in the reaction of different children may be accounted for by such things as differences in exposure to light, rate of growth, etc. Nevertheless, there is certainly an individual factor which enters into the etiology of the disease in children. It must be remembered, however, that the food which is given an infant in his bottle is not necessarily identical with the pabulum which is absorbed from the gastro-intestinal tract. It may be that the dietary maladjustment may take place during the passage of nutritive substances from the lumen of the gastro-intestinal tract into the body.

Park has very recently suggested that at present rickets must be regarded as a deficiency disease which is the product of an insufficient supply of the anti-rachitic substance and of irradiation.

Perhaps in the light of recent work which has been done to investigate rickets the theory of von Hanseman will eventually remain prophetic of the actual cause. This is the "theory of domestication." In brief, according to this theory, rickets is a part of the price which man and certain animals pay for the deviation from the habits of their ancestors which is known as civilization or domestication. These words are used to represent the changes in dietary and hygienic habits necessitated among human beings by the assumption of community life, and among animals by enforced or voluntary association with man.

TREATMENT

The means by which rickets may be healed are evident from the foregoing account of the disease.

SPECIFIC THERAPEUTICS

While no doubt the time will come when it will be possible by intensive study to determine the factor or factors which are operating to produce rickets in each individual case, that time is not yet. We have fortunately, however, as has been indicated above, at least two specific treatments for rickets. One is the administration of *cod-liver oil,* the other exposure of the patient to radiation with certain of the shorter *light rays.*

Cod-liver Oil.—It has been usual in the past to give cod-liver oil in combination with elemental phosphorus, and such studies as those of

Schabad had convinced the profession that this combination was efficacious in promoting calcium retention in the body and healing of the rickets. Recent studies which have been carried on have led us to doubt the value of elemental phosphorus in the amounts usually given in causing healing of rickets. Cod-liver oil cures the disease. The addition of phosphorus to the oil is of doubtful value at best. As regards the choice of the oil to be used, the commercial Norwegian (Lofoten) oils are at present not as good as those carefully made from North American cod. The antirachitic substance in the fish oil is quite resistant to heat and oxidation. The more elegant preparations of cod-liver oil, such as the hydroxyl-free oil and the various emulsions which are on the market, have not yet been tested for their antirachitic potency. The oil may be given in amounts ranging from 10 minims to 15 minims (0.5 to 1 c.c.) four times a day to a rachitic infant of one year old with certain curative effect. Many children will tolerate much larger quantities (up to 3 ss—2 c.c.) four times a day. Diarrhea with the passage of four or five loose yellow stools a day is not necessarily a contra-indication. Healing begins in from two to five weeks. There are other fish oils such as Menhaden oil which are more potent antirachitics than cod-liver oil but these are not as yet on the market.

Short Light Rays.—Treatment with short light rays may be given with either the sun or the mercury vapor lamp. The rays derived from the chromium iron or cadmium (Shipley) or carbon (Hess) arcs are curative, but the mercury vapor and the carbon arc lamps are most readily obtained and easily used. Rickets may be treated by exposure to sunlight anywhere. However, since the potency of the light depends on rays of very short wave-length which are readily filtered out by fog and moisture, exposure in situations where the sunlight is most actinic will be most rapidly beneficial. Hence the mountains of middle range and the seashore in equable climates afford prospects of the most rapid cure. In these situations the children may be gradually accustomed to exposure to the sun until they can bear it nearly or quite unclad.[1] Due care must be taken to prevent burning of the skin. The exposure must not be made through glass as this filters out the beneficial rays.

Mercury Vapor Lamps.—Treatment with the mercury vapor lamp is best carried out with the Alpine sun lamp. There is some confusion about the technic of applying ultraviolet therapy.[2] Huldschinsky recommends an initial exposure of 5 minutes at a distance of 32 inches. This time of exposure may be increased by 2 minutes at each successive treatment, until 20 minutes is attained. The distance may be decreased gradually to 28 inches. According to Pacini the beneficial rays are those

[1] See article by Pryor, Vol. II, page 670.—Editor.

[2] All of the observers quoted have used lamps of different make and pattern. Huldschinsky's lamp is probably the "Sollux." That used by Pacini was a lamp made by the Victor Corporation. The "research lamp" referred to was made by the Hanovia Chemical Company.

in the ultraviolet spectrum from 3,022 to 2,900 Angstrom units. In order to derive the maximum intensity of light in this region from the mercury vapor lamp, he suggests that the lamp should be 40 inches from the patient. The voltage should be so adjusted so that the voltmeter reads 70. He gives an initial exposure of 15 seconds to a dark infant with the tube directly above the child. The treatment which has been found effective at the Johns Hopkins Hospital has been given with a small "research type" air-cooled mercury lamp. Children are radiated from a distance of 18 inches. Radiation is given daily. The initial time is 5 minutes; this is increased by 5 minutes on alternate days until 20 minutes is attained. Radiation is continued daily until the roentgenogram shows advanced healing. This lamp uses a direct current of 4 amperes. When the ultraviolet light is used, the patient's eyes should be protected by bandages or by amber goggles since this light causes a painful conjunctivitis and may, if this warning is disregarded, eventually cause an opacity of the vitreous humor and permanent blindness. Exposure of the entire body is not necessary. Radiation of a single limb is sufficient to establish a cure. Cod-liver oil may be given with advantage during and after the period in which the child is irradiated. The same doses of the cod-liver oil may be given as those used when light therapy is not employed.

Radiation with ultraviolet light and the administration of cod-liver oil may be controlled by roentgenograms of the ends of the long bones, and examinations of the blood-serum. Therapy should be continued until complete calcification of the metaphysis has taken place.

Auxiliary Therapy.—While cod liver and radiation are specific in the treatment of rickets, the diet should be so regulated as to be as nearly non-rickets producing as is possible. With this end in view, the patient should be given a formula of whole milk and water, with or without additional sugar, appropriate to his age. As rapidly as possible the diet should be supplemented with eggs and with purées containing ample amounts of leafy vegetables, in addition to such vegetables as carrots and peas which have of themselves no antirachitic value. Such a purée may be added to the diet of an eight-month-old child with great profit and without danger. Scraped raw beef is of value also. Children of one year or over should be persuaded to take a soft mixed diet as rapidly as possible. The following will serve as an example of such a diet:

DIET

6 A. M. Cereal (cooked), 1 to 2 ounces.
1 egg (boiled soft).
Milk, 4 ounces.
A part of the milk may be poured on the cereal at breakfast and supper.

8 A. M. Orange juice, 1 ounce.
10 A. M. Toast with butter or milk toast, 1 slice.
2 P. M. Soup or broth, 2 to 4 ounces.
Scraped beef, ½ to 1 ounce.
Potatoes or substitute, 1 to 2 ounces.[3]
Green vegetables, ½ to 1 ounce.
Milk, 4 ounces.
6 P. M. Cereal, 1 to 2 ounces.[4]
Bread and butter or toast, 1 slice.
Stewed fruit, ½ to 1 ounce.
Milk, 4 ounces.

Rickets will heal slowly on such a diet even without the use of specific therapy. The physician should take care to see that raw fruit juices are taken daily to avoid the danger of scurvy, although they have no antirachitic effect in the proportions in which they are usually fed.

Hygiene.—The rachitic child needs fresh air and exercise even more than does the normal one. If it is feasible, the child should be taken out of the city into the mountains or to the seashore in a mild equable climate. It is perfectly possible, however, to treat rickets in the city by keeping children out of doors in the fresh air as much as the weather allows. The clothing should protect the child from chilling but the sun should be allowed access to as much of the skin as the weather will permit. The child should sleep in a room with wide open windows, and rooms occupied by it in the daytime should be well aired.

Other Means of Treatment.—*Cold bathing* has been recommended as an aid to treatment. The child should be accustomed as rapidly as possible to have sponge baths with water at 50° F. These should be given every morning. Salt baths have been recommended and are well tolerated.

Massage in very young children is a good substitute for exercise and should be begun immediately treatment with cod-liver oil is started.

It is probable that it is unnecessary to treat the *special manifestations* of rickets individually. The rapid cure of the *anemia* of scurvy by orange juice may be considered as indicating that the rachitic anemia will clear up under the influence of antirachitic treatment alone. However, some preparation of *iron* may be given at the discretion of the physician. The saccharated carbonate is the best preparation of this drug.

Atropin has been recommended to control very profuse perspiration in doses of $^1/_{800}$ gr. Its use is unnecessary and unwise.

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[3] Spaghetti, macaroni or rice may be substituted for potatoes at will. Vegetables include carrots, peas, kale, spinach, string beans, beets, squash, lima beans, cauliflower, or cabbage.

[4] In view of the marked antirachitic effect of egg yolk, a cereal may be made up with an egg as was the so-called "frumenty" which was a staple food among the country people of England for centuries. The latter was made from wheat, cream, or milk, and eggs and served with spices and powdered sugar.

COMPLICATIONS

Rhinopharyngitis, bronchitis, and bronchopneumonia, when they complicate rickets, should be treated with extreme care in accordance with the rules elsewhere given.

Rickets with Tetany.—It is now generally considered that tetany in its various manifestations (convulsions, carpopedal spasm, latent tetany, etc.) is closely associated with rickets under certain conditions. While there can be no doubt that tetany may in certain instances result from overventilation of the lungs or other conditions which tend to bring about alkalosis, almost every case of tetany in infants is the result of disturbances in metabolism closely allied to or the same as those which produce rickets. It has been stated that tetany is a phenomenon which accompanies the healing of the rachitic process. This is sometimes the case and, indeed, it is probable that under certain conditions the healing of rickets may initiate the tetanic attacks. However, this is not the usual modus operandi. In very few children does tetany accompany the healing of rickets. The studies of Howland and Kramer on the blood of rachitic children have shown that the reduction of the numerical value of the product of the amounts of the inorganic phosphate and calcium of the serum below 40 is an infallible criterion of the presence or absence of rickets in children. It is quite clear that this product may be so lowered as to fall within the rachitic zone if either the amount of calcium or inorganic phosphorus of the serum is sufficiently reduced. It is equally obvious that the concentration of either of the above-mentioned substances in the blood of the rachitic child may vary within definite limits. Howland and Marriott have shown that the calcium content of the blood-serum of children with rickets complicated by manifest or latent tetany falls from the normal to as low as 3.5 mg. per 100 c.c. of serum. The exhibition of calcium is followed by immediate elevation of the serum calcium and the cessation of the manifestations of the disease. It is only necessary then to regard the majority of instances of tetany in infants as the accompaniment of rickets in which the calcium of the serum is sufficiently reduced and as caused by the same metabolic disturbance. It is notable that tetany is most liable to occur in the course of mild rickets and of rickets in premature children.

Tetany may be either active when it manifests itself by convulsions, or carpopedal, or laryngospasm, or latent in which event its presence is recognized only in the course of an electrical examination or by the results of the determination of the calcium of the blood-serum.

The course to be pursued in treating tetany depends on whether or not the afflicted child is having convulsions. Latent tetany or tetany which is indicated only by carpopedal spasm or increased facial sensibility

may be treated by the administration of calcium salts. Calcium may be given as the chlorid in doses of from 5 to 10 gr. three times a day. If the lactate is used the dose should be doubled. Calcium therapy is, however, only palliative and unless antirachitic treatment is instituted coincidently the elevation of the calcium in the serum which follows its administration is not maintained. Cod-liver oil should be given as in the treatment of uncomplicated rickets. The use of this oil alone will slowly raise the level of the calcium in the serum and will cause the rise which follows lime salt therapy to be permanent. The exhibition of the oil should be continued after calcium medication has been withdrawn. The withdrawal of calcium may be cautiously begun after about two weeks. Latent or border-line tetany may be treated successfully with ultraviolet light (Howland, Kramer and Casparis).[5] Palliative therapy against tetany with ammonium chlorid in doses of 3i to iss (4 to 6 gm.) has been recommended and successfully used on animals. This procedure is, at present, only in the experimental stages and is not yet to be recommended for clinical use.

Convulsions occurring in the course of tetany demand immediate symptomatic treatment. Severe, frequently recurring convulsions may be controlled with chloroform inhalations. For those which are less severe the mustard bath or pack may be tried. These procedures may be followed by the hypodermic administration of morphin ($^1/_{60}$ to $^1/_{20}$ gr. according to the age of the child) or anhydrous magnesium sulphate (2½ to 7½ gr.). Chloral hydrate (2½ to 5 gr.) may be given either by mouth or rectum. The bromids have no value in the treatment of tetany. Laryngismus sometimes demands artificial respiration or a few whiffs of chloroform. The minor manifestations of tetany in older children, cramp or carpopedal spasm may be temporarily relieved by warm baths and massage.

Treatment of Rachitic Deformities.—The deformities which result from rickets are repaired in a surprisingly large measure by nature once the active disease has become healed. Even the most badly deformed children can be expected to improve very considerably. Treatment of the deformities should nevertheless be undertaken before the healing of the rickets is complete. The muscles of the limbs and trunk should be massaged for half an hour each day with a hand anointed with coconut oil. At the same time the deformed extremities should be manipulated. Manipulation is best carried out by grasping the affected limb in both hands, one hand near each end, and subjecting it to pressure applied as though to straighten the bone. The pressure should be gentle and great care must be taken not to break the bone. Pressure should be made and released quickly (at intervals of about one second) twenty times on each bone twice a day.

[5] Unpublished observation.

Residual deformity, after healing is complete, should be treated by osteotomy. This operation may be done at any time in early childhood after the third year.

Fractures of rachitic bones should be treated on general surgical principles.

The use of braces in the correction of deformities from rickets is to be condemned. Braces prevent the muscles from exercising their normal functions and so from regaining their normal tone.

Teeth.—Since the teeth of rachitic children readily become carious and often develop malocclusions, their care should be placed in the hands of a competent dentist immediately after their eruption.

PROPHYLAXIS

The prophylaxis against rickets consists of the employment of the same measures recommended above for therapy in curative therapy. It consists of a diet proper to the age and digestion of the child, fresh air, hygiene, and exposure to the light of the sun out of doors. Cod-liver oil may be given if necessary in small doses, but under ordinary conditions healthy children will be best and most easily protected by proper diet and hygiene. The premature cannot be expected to tolerate cod-liver oil and such a child cannot be taken out of doors. It would no doubt be beneficial to these children to receive small doses of ultraviolet radiation.

REFERENCES

Glisson, F. De rachitide sive, etc. London, 1650.
Dibbelt, H. Verhandl. d. deutsch. path. Gesellsch., xiii, 1909.
Findlay, L. Journ. Path & Bacteriol., xxiii, 496, 1920.
Hess, A. F., and Gutman, M. B. Journ. Am. Med. Ass., lxxviii, 29, 1922.
Howland, J., and Kramer, B., Monatschr. f. Kinderh., xxv.
——— Am. Journ. Dis. Child., xxii, 105, 1921.
Howland, J., and Marriott, W. McK. Quart. Journ. Med., No. 44, xi, 1918.
Huldschinsky, K. Ztschr. f. orthop. Chir., xxxix, 426, 1920.
Hutchinson, H. S., and Shah, S. J. Quart. Journ. Med., xv., 167, 1921-1922.
Kramer, B. and Howland, J. Johns Hopkins Hosp. Bull., xxxiii, 313, 1922.
Kramer, B., Casparis, H., and Howland, J. Am. Journ. Dis. Child., xxiv, 20, 1922.
Matti, H. Ergebn. d. inn. Med. u. Kinderh., x, 1, 1913.

McCollum, E. V., Simmonds, N., Becker, J. E., and Shipley, P. G. Journ. Biol. Chem., liii, 292, 1922.

McCollum, E. V., Simmonds, N, Parsons, H. T., Shipley, P. G., and Park, E. A. Ibid., xiv, 333, 1921.

McCollum, E. V., Simmonds, N., Shipley, P. G., and Park, H. G. Ibid., li, 41.

Mellanby, E. A. Privy Council Med. Research Council, Special Report Series No. 61, London, 1921.

Morpurgo, B. Centralbl. f. allg. Path. u. path. Anat., xiii, 113, 1902.

Pacini, A. J. Outline of Ultraviolet Therapy, Chicago, 1923.

Park, E. A. Physiological Reviews, iii, 106, 1923.

Park, E. A., and Howland, J. Johns Hopkins Hosp. Bull., No. 369,341 xxxii, 1921; xxxii, 101, April, 1921.

Powers, G. F., Shipley, P. G., Park, E. A., McCollum, E. V., and Simmonds, N. Journ. Am. Med. Ass., lxxviii, 159, 1922.

Shipley, P. G., Park, E. A., McCollum, E. V., and Simmonds, N. Journ. Biol. Chem., No. 2, xlv, 1921.

——— Johns Hopkins Hosp. Bull., xxxii, 160, 1921.

——— Am. Journ. Dis. Child., xxxvi, 335, 1922.

Soranus of Ephesus. ΠΕΡΙ ΓΥΝΑΙΚΕΙΩΝ ΠΑΘΩΝ. *κεφ.* λη.

CHAPTER IX

PELLAGRA

EDWARD JENNER WOOD

Much progress has been made in the management of pellagra resulting from the study of its etiology. This progress has been achieved in spite of a division on the part of the students of the disease. One school still regards it as an infectious disease, the specific cause not being known, while the other school considers it a disease of food deficiency. Even among the latter there is by no means unanimity as to the exact nature of the food fault. The rôle which maize has so long played in the disputes regarding the etiology of pellagra has been overshadowed by many intricate problems of a more modern kind. It was only to be expected that the maize theory would die a natural death for the simple reason that the disease occurred among people not using the cereal in any form. The valuable contribution made by the maize study is the development of the knowledge that this grain like rice (and also like wheat as shown by Little and Ohler) has its antineuritic substance situated in a part of the kernel which is removed in the process of modern milling. It seems reasonable that if Lombroso had substituted the word *deficiency* where he used *toxicity* his writings would have had a different effect. The germ of maize contains the antineuritic substances and this germ is situated at the hilus. It is quite soft and much more readily subject to the damages done by molds, mites and rats. However, the solution of the causative factors of this disease seems not to rest in the mere finding of an antineuritic factor.

Two notable contributions to the study of the etiology have been made which do not depend on a food deficiency.

Jobling and Peterson studied pellagra in Nashville, making an exhaustive epidemiological investigation which calls for the most earnest consideration.

It was shown by these observers that 78.8 per cent of the patients gave definite histories of previous exposure to the disease. They were impressed with the fact that the new cases developed only in individuals who lived near or associated intimately with pellagrins. They thought

that the conclusions that pellagra was a metabolic disturbance were inconclusive and by no means final and that much more animal experimentation and epidemiological study would be needed to settle the question.

Pellagra has been repeatedly regarded as a disease of "place" and the situation in Nashville did not differ materially in this regard from that in Italy. This grouping of cases has led to a correlation between the topography and geology of the country and the incidence of the disease. The Italians have called attention to more cases and more severe cases in certain districts than in others regardless of differences in economic and hygienic conditions.

The Nashville experience regarding "place" relationship is not universal. In the early days of the occurrence of pellagra in North Carolina the writer recalls many cases occurring sporadically in isolated places far removed from other like cases and occurring where the disease was utterly unknown, unsuspected and unassociated with anything ever seen before by both laity and medical profession. In those days many patients were examined who stated emphatically that they had never been thrown with the disease, had never seen it before and, in many instances, had never heard of it.

The contributions of the Thompson-McFadden Pellagra Commission are of great value though one may not agree with their conclusions. The work was a carefully arranged scheme of field work in Spartanburg, South Carolina, where conditions for first hand study were admirable. The Commission was made up of experts in the various fields of medicine and the allied sciences, including all divisions of work which might have a bearing on the discovery of the cause of pellagra.

In the first report of this Commission the following conclusions were reached:

1. The eating of sound or diseased maize has no causative relationship.
2. The disease is in all probability a specific infection communicable from person to person by means unknown.
3. There is no evidence incriminating a biting insect as an intermediary.
4. Intimate association in the household and contamination of the food with the excreta of pellagrins are regarded as possible modes of transmission.

General hygienic improvement, as the installation of a water carriage system of sewerage, was thought by the Commission to have been attended by a decided improvement in the pellagra situation. Vedder reviewing the work accomplished on the field concluded that there was nothing in the evidence against the conclusion that the improvement was brought

about by food changes. In spite of this failure to agree with the findings by a recognized authority on food diseases, the fact remains that the work of this Commission forms one of the most valuable contributions to the study of the epidemiology of the disease and the data are most valuable.

Louis W. Sambon advanced the theory of an intermediary of the Simulidæ group in the transmission of pellagra, but the acceptance was made impossible by the failure to find Simulium in certain places, such as Barbadoes, where pellagra was rife. Sambon still believes that the disease is insect borne and is disposed to believe that another group, such as the Culicidæ, may be incriminated when the matter is further investigated.

Sambon does not regard the improvement in the pellagra situation in the southern states to be due to food improvement, but cites instances in Italy where the same variations have occurred which were in no way connected with a failure in crops or other economic vicissitudes. This matter needs further investigation. For the present there is every reason to believe that attention to the hygiene of foods has had much or all to do with making pellagra a rare disease in those sections of the United States where ten years ago it was a veritable scourge. Whatever can be said for or against the food theory of to-day does not alter the fact that in a century and a half no theory has been brought forth the practical application of which was attended with such immediate and magical amelioration of a very desperate situation. Before the food reform was suggested the outlook in the southern states was no different from that of those sections of Italy which have been despoiled by a degenerating disease which was not understood and therefore uncontrolled.

During the War pellagra was not accepted as an excuse for the draft. Service in the American army proved a splendid cure.

PROPHYLAXIS

Prophylaxis is now and will continue to be the most important phase of the subject, just as it is in scurvy and beriberi. It has been proved that certain hygienic reforms will prevent the appearance of the disease. These reforms have had to do with change in food selection as well as in food preparation. But in addition to these improvements it has been believed by the advocates of an infectious cause that better sewage disposal has played a great part also. The evidence would tend to indicate that in certain instances where the only change brought about has been in the improvement of food the disease has been seen to disappear completely and permanently. No evidence seems to be forthcoming, tending to prove that a water carriage system of sewerage alone, without other

improvements, was sufficient to prevent the continued occurrence of the malady.

Indian corn or maize was first connected with pellagra by the work of Marzari in 1810. It was the work of Lombroso, however, which focused attention to it and through his study many accepted his view that damaged corn caused pellagra. He regarded it as an intoxication resulting from the products of the life activity of certain molds which in themselves were harmless. He believed that moisture played a large part in the process and, acting on his suggestion, the Italian Government undertook the drying of corn by artificial means. Evidence has been piling up against Lombroso's claims ever since the first expression of them until to-day few observers are left to defend them.

Ceni taught that the Aspergillus flavescens and the Aspergillus fumigatus were the direct cause and demonstrated their presence in diseased corn. Tizzoni isolated from the blood, the feces, the cerebrospinal fluid and organs at autopsy—an organism which he regarded as the specific cause but his claims have not been verified. In spite of the fact that, in the hands of such competent observers as Lombroso, Tizzoni, Cuboni, Ceni and many others, certain changes were produced in laboratory animals—such as the falling out of feathers in fowl and of hair in rabbits—we were ignorant regarding the appearance of pellagra experimentally produced except in man, as was recently done by Goldberger, though it must be remembered that this claim of Goldberger has not been universally acknowledged to be correct. The exception to this statement is the case of a monkey in the Lister Institute in London. The writer was shown this animal by Miss Hume and was personally satisfied that the erythema and other symptoms were due to pellagra. It is especially worthy of note that the symptoms were produced in the same manner as were the symptoms in man by Goldberger, namely, a faulty, one-sided diet.

The work of Goldberger and his associates of the United Public Health Service is to the writer's mind the most important work yet done in the study of the etiology of pellagra. It at once supplies a definite plan of prevention. These observers studied various types of institutions, such as insane asylums and orphan asylums, in the "pellagra area" and found that a correction of the diet invariably wiped out the disease without any other change. Milk was found to be a splendid prophylactic measure and also, in a measure, a curative agent. The smaller children in the institutions studied were found to have escaped when the number of cases was great. This escape was thought by Goldberger to have been due to the fact that such inmates were given milk while the other children were not.

As stated above, Goldberger then attempted to produce the disease experimentally in man by a faulty diet. According to his opinion and that of a number of observers who were quite familiar with the clinical manifestations of the disease, the symptoms produced were pellagra. Because

of the distribution of the skin lesions on certain covered portions of the skin, objection was raised to regarding the disease produced as pellagra. The chief contention was the skin lesion of the scrotum. The writer has been much interested in this phase of the subject and has collected from his own hospital experience a number of photographs showing the lesion of the skin of the perineum and about the vulva. Besides this he has seen many instances of scrotal lesions. In fact, this very contention has resulted in demonstrating the importance of a study of the whole skin surface in suspected pellagra. He recalls one case with only an insignificant perianal involvement of skin in an otherwise typical case. The degree, the extent and the distribution of the skin surface involved is in no way any indication of the extent of the disease. The occupation and habits have much to do with the amount of skin lesion and its location. The action of the sun certainly affects the location as well as the extent of the skin lesions. In the light of this experience, this objection to Goldberger's conclusions, which seem quite reasonable, appears quite without suitable foundation.

Quite recently Goldberger and Tanner have been more specific in pointing out the deficiency which they believe to be the cause of pellagra. They state that persons receiving a varied diet for a number of months might develop the disease. Even in cases where considerable amounts of vitamin-rich foods of every class have been consumed the disease has occurred. In such cases the mineral elements equal to that in a liter of milk were added. They have reached the conclusion that pellagra is due to an amino-acid deficiency and suggest that this explains those rare instances of pellagra in breast-fed children in which cases the amount of the amino-acid elements were insufficient or there occurred a faulty utilization of the amount consumed.

The work of Goldberger and Tanner in essentials is strikingly similar in its conclusions to that of the Egyptian Pellagra Commission. The latter work was based on the observation of 2,000 German, Austrian and Bulgar prisoners of war at Maadi. For two years these prisoners occupied a compound immediately adjoining that of 6,000 Ottoman prisoners. Living conditions were the same except that the smaller group supplemented prison fare with occasional outside purchases of food. No cases of pellagra occurred among the smaller group while among the Ottoman prisoners 300 were recorded in a single year. It was found that there was a definite connection between bodily activities and the development of the disease. The Commission reported that they found "that the food issued to both labor and non-labor prisoners provided an ample margin over the requirements of healthy men, and gave a suitable balance of proximate food principles, but the biological value of protein fell below the amount which the researches of the Committee established as a new minimum for the prevention of pellagra." They particularly emphasized

the importance of the utilization of protein as a means of prevention and referred to such conditions as diarrheal diseases as predisposing factors in causation because of the great loss of essential nutritional elements before utilization could occur. Wilson and Roaf, members of the Egyptian Commission, have emphasized the fact that an individual may be susceptible to the disease because of an error of metabolism and that the predisposed subject may or may not develop the disease according to whether or not he is at rest or at physical labor. It was noted that in diarrheal diseases the protein absorption might be reduced to as low a point as 67 per cent.

In the light of such illuminating study as the above it is not now so difficult to explain numerous cases which hitherto seemed irreconcilable with a dietetic error or deficiency. Enright reported that in 1919 a number of German prisoners in Egypt developed acute symptoms of pellagra though, according to their statements, an ample protein dietary had been received before their capture in Syria as well as during the four months of imprisonment in Egypt. At this same time it was noted that pellagra had not been seen in extensive outbreaks in the half-starved hordes of central Europe. Before counting this an argument against the food theory, such cases must be analyzed carefully on the merit of each individual case, keeping in mind Goldberger and Tanner's recent work in the amino-acid explanations and also the work of the British observers in the Egyptian reports.

One can hardly ignore the argument of the opponent to a food explanation which refuses to accept a deficiency theory because starvation has never been shown to cause pellagra. Again, many of the Asiatic peoples eat practically no protein food and yet escape pellagra. One, too, finds difficulty in getting away from the apparent simplicity of cause and effect in the experience of P. A. Nightingale in Rhodesia. In a prison an acute disease appeared unknown to the observer but the diagrammatic sketches of the skin lesion and the account of the symptoms show very definitely the disease picture of typical pellagra. At once Nightingale was convinced that the fault was of food origin. In former times ropoka, a small variety of maize, was grown in the prison farm and was hand ground in toto by the prisoners. During all the period of this plan of feeding no pellagra had been seen. When the ropoka crop failed the prisoners were fed on "mealie meal" which was a form of meal made from maize rendered deficient by the manner of commercial milling. As soon as the return to the original food was made, the result in the prison from the standpoint of stamping out the disease was, in the language of the observer, "immediate and magical."

Impressed by the experience of Nightingale, the writer investigated the commercial meal commonly sold in the South and found that in the modern steam mill the corn is "degerminated." The germ of maize

is situated at the hilus of the kernel and this germ contains so much fat that the process of removal has been made necessary in order to prevent rancidity. It will be recalled that the Philippine work on rice in the production of beriberi was done on the assumption that phosphoric acid was a reliable indicator of the antineuritic substance. It was not claimed nor thought that the phosphorous body had any property of its own in this respect. In a study of maize and the changes brought about in its milling the writer used the same indicator without assuming that the nature of the deficiency causing beriberi was the same as that causing pellagra. The following table shows the results.

	Percentage of P_2O_5
Maize germ with bran	1.5
Maize meal ground in toto	0.78
Highly milled maize meal without germ	0.29
Maize meal without germ not highly milled	0.58

A specially prepared maize germ without bran which contained over 2 per cent of P_2O_5, was supplied for experimental purposes by the Ballard & Ballard Milling Company.

Extensive feeding experiments on pigeons were made to find out the part played by milling in the nutrition and growth. It was found that polyneuritis was readily produced by a product low in P_2O_5 just as was the case in polished rice.

A study of a small village where much pellagra had occurred brought forth the fact that the abandonment of the old water grist mill, to which the people carried small amounts of maize to be ground and which was consumed within a few days, was coincident in point of time with the appearance of pellagra. For the old product, which was the whole kernel with no germ or bran removed, was substituted a highly milled product with germ removed. In addition to this modern innovation at about this time highly milled wheat flour was introduced in that mixture known as "self-rising flour" which contains bicarbonate of soda and acid sodium phosphate. Experiments with baking powder showed that frequently the end product after heating was decidedly alkaline. It will be recalled that Voegtlin showed the harmfulness of an alkaline medium in the cooking of food. This harm seemed to be in a destruction of the protective substances commonly called vitamins.

In the cotton-mill villages of the South where pellagra was rife it was the common practice for the people to live on highly milled cereals cooked with baking powder or its equivalent, the self-rising combination, to put sodium bicarbonate in the vegetables to cause quick cooking and tenderness, to eat the white salt pork as the only meat except on Sundays, to drink strong coffee without milk at any time and seldom to eat eggs. All of the errors which have been pointed out by the various workers can

be found in this plan of life, but there is much to suggest that the type of meal or flour used has not received sufficient attention. An important point is a careful consideration of the time relationship between the introduction of these perversions of diet and the appearance of pellagra. The grandparents of these people ate cornmeal and wheat flour ground at the local mill with no removals and it was cooked in the ashes without rising agent of any sort. They also ate smoked pork where to-day the salt pork is eaten. These people never had pellagra, not even in the lean years immediately following the Civil War nor during that war when the country was in the hands of the enemy and extreme privation was suffered.

TREATMENT

Regardless of what view of the etiology one may espouse, the fact remains that until all the forces were directed towards the dietary no results were obtained in treatment. With the adoption of the principles of diet reform indicated in the work of any student of the disease of the present or of all the students (for there is little practical difference) striking results may be expected provided the disease has not existed unrecognized until structural nervous change has occurred.

Milk is the greatest prophylactic and the greatest cure. Indeed, it almost approaches to being a specific. It is inconceivable that pellagra could develop in an individual consuming a reasonably sufficient amount of milk. Fresh beef and other fresh meats not overcooked rank next in the writer's list. Too much importance cannot be attached to the free and abundant use of fresh salad vegetables, not overcooked and not cooked with fat meat and alkalis. Fresh fruit must be included in the list. The writer stresses the use of whole wheat flour or whole cornmeal though he appreciates that there is no final conclusion on this matter and many capable observers regard his views as of no value. It is certainly important from every possible point of view to avoid chemical rising agents and highly milled grain.

Among well-conditioned people pellagra occasionally occurs and in such cases it will usually be found that the victim is given to unnatural likes and dislikes in food, the fault of which is readily detected and the needed change easily made with the coöperation of the patient. It is in such cases that one should remember Goldberger's teaching that it is not what is on the table but what the patient actually eats which determines the liability to pellagra. Among the aged, especially when they are living alone with no younger people to take an active interest in the menu, pellagra frequently occurs. The writer has encountered a number of cases in elderly men living alone and preparing their own food. Having

no appetite and no interest in food they frequently lapse into unnatural food habits because of the ease of it and the disease develops.

It has been noted from the beginning of our American experience with pellagra that the diseases lowering general resistance are definite predisposing factors and must be removed at the very start. In the South one of the chief of these is uncinariasis. The incidence of pellagra in North Carolina is now so much reduced that when a case presents itself it is a reasonable conjecture that some intestinal parasitic or diarrheal disease will be found. The last case under the writer's care is a man with a severe bronchiectastic condition. His manner of life is such that it is reasonable to believe that some debilitating influence must have played a predisposing part. The child-bearing process is a vital predisposing factor especially when the patient is already below par from some of the above-mentioned conditions. A fertile source of the disease of considerable importance is the present vogue of a low protein diet in the cardio-vascular-renal group of diseases. This source of danger can be eliminated when the patient is allowed milk.

In the light of the experience of the writer in the use of the germ of maize as well as with the cortical portions of wheat in the relief of experimental polyneuritis, an attempt was made to relieve pellagra in the same way.

In one instance an elderly white man was admitted to the ward on Tuesday afternoon. On Wednesday he was placed on an exclusive diet of maize germ, allowing him butter only as an addition. No drugs were given. On Sunday he left the hospital with all symptoms relieved and had no recurrence after two months. This patient had suffered from diarrhea for several months. Two days after the treatment began he was constipated. The erythema cleared up as if by magic and the mild stomatitis promptly disappeared.

A second case was admitted and the same plan of treatment tried. The patient had a bullous erythema, stomatitis and diarrhea. In addition to this disease he had diabetes. After four days the pellagra symptoms disappeared and a little later the Allen fast was instituted with good results and no return of pellagra symptoms.

An old negro in the last stages of the disease, with marked mental changes, a diarrhea which extended throughout the year, marked skin lesions and stomatitis, failed to recover under this treatment. While the distressing symptoms of the mouth and skin were relieved, the diarrhea continued and he finally succumbed.

A negro woman of thirty years, with incontinence of bowel and bladder, advanced dementia, extreme degree of skin involvement and stomatitis, was fed by the stomach tube, three times in twenty-four hours. At each feeding she was given 1 pint of milk, 3 eggs and 4 ounces of a wheat middlings gruel. The maize germ could not be given through the tube, hence

the substitution of wheat. The patient improved in every way except mentally. The diarrhea was greatly improved and the skin and mouth symptoms cleared up. She died suddenly of an unexplained cause. It is notable that there was no improvement until the cortical grain element was added to the feedings. Milk, eggs and lactose had failed to relieve the symptoms.

Maize germ is known commercially as "corn chops" in North Carolina and is sold as cattle food, being famous as a good milk producer. In the section where the writer's observations were made it has been used extensively by pellagrins and the results have been more encouraging than with anything else tried, though it is always insisted on that milk, rare beef, eggs, green vegetables and legumes be added to it. When the patient's mouth is painful and swallowing is difficult, a gruel may be given with milk and eggs.

From Coletti and Perugini, Lombroso revived the use of arsenic in pellagra. Ever since it has had the greatest vogue and is still extensively used. Fowler's solution, soamin, atoxyl and, more recently, cacodylate of soda have been vaunted by various observers. The writer has not been convinced that the result is any more than the tonic effect though the patients always claim improvement in feeling after the injections. There are two obvious objections to arsenic, especially the forms given hypodermically. The first is the danger of increasing the dose beyond safe limits in a desperate situation which cannot be greatly helped thereby. The second is the sense of false security which results ofttimes in the ignorant patient neglecting the weightier matter of proper nutrition and pinning all faith in the drug.[1]

Finally, rest and quiet until all active symptoms have disappeared is most helpful.

REFERENCES

Boyd, F. B., Roab, H. E., et al. Report of a Committee regarding the Prevalence of Pellagra among Turkish Prisoners of War, Journ. Roy. Army Med. Corps., London xxxiii, 447, 508, 1919; xxxiv, 70, 1920.

Ceni, C. Richerche sul potere reproduttivo e sull' ere ditarieta nella pellagra sperimentale, Riv. sper. di freniat., Reggio-Emilia, 1901.

——— Gli aspergilli nell' etiologia e nella pathogenesi della pellagra, Ibid., 1902.

Dyer, I. Quoted in Stitt's Tropical Diseases.

Enright. Lancet, May 8, 1920.

Goldberger, J. Pub. Health Rep., June 24, 1914; Sept. 11, 1914; Oct. 23, 1914; Jan. 15, 1915.

——— Journ. Am. Med. Ass., Oct. 10, 1914; Feb. 12, 1916.

[1] Atoxyl should certainly not be given on any account. It is a dangerous preparation and not infrequently causes optic atrophy.—Editor.

Goldberger and Tanner. Ibid., Dec. 23, 1922.
Jobling and Petersen. Journ. Infec. Dis., xviii, 501, 1916.
Little, J. M. Journ. Am. Med. Ass., lviii, 1912; lxiii, 1914.
Lombroso, C. Sull' eziol. Ogia e sulla cura della pellagra, Lavori d. Cong. di med. int., v, Milan, 1892.
Marzari, G. B. Saggio-medico-politico sulla pellagra, o scorbuti italico, 8, Venezia, 1910.
Nightingale, P. A. Transvaal Med. Journ., vii, 261, 1912.
Ohler, W. R. Journ. Med. Research, xxxi.
Tizzoni, G. Intorno alla Pathogenesi ed Etiologia della Pellagra, Contributo Batteriologico e sperimentale, Roma, 1909.
Voegtlin, Sullivan, and Myers. Pub. Health Rep., April 14. 1916.
Wood, E. J. Journ. Am. Med. Ass., May 16, 1916.
——— Tr. Ass. Am. Physicians, xxxi, 99, 1916.
——— Am. Journ. Med. Sc., clii, 813, 1916.
——— Oxford Medicine, ch. xiii, 1920.

DISEASES OF THE GLANDS OF INTERNAL SECRETION

CHAPTER X

DISEASES OF THE ADRENALS

FREDERICK FORCHHEIMER AND FRANK BILLINGS

REVISED BY GEORGE BLUMER

ADDISON'S DISEASE

In 1855 Addison described not only the symptom-complex of this disease but its cause as well: "Disease of the suprarenal capsule." In human beings it may be considered, as far as its pathological basis is concerned, under two headings: (1) The primary form, due to atrophy, hypoplasia, or cirrhosis of the adrenals. (2) The secondary form, due to tuberculosis, syphilis, or tumors (Bittdorf). In by far the greatest number of cases tuberculosis of the adrenals is found.

In the present state of our knowledge we are forced to the conclusion, notwithstanding pigmentation of the skin is not explained by it, that in all cases of Addison's disease there is a deficit of adrenal tissue. Whether this tissue is medullary or cortical, or both, is not determined as yet.

TREATMENT

Organotherapy.—Under these conditions we would necessarily come to the conclusion that, in order to keep internal secretion normal with insufficient tissue, something might be introduced into the economy, as is done in thyroid gland insufficiency. Organotherapy was probably first employed in this disease by Charrin and Langlois in 1894 by the subcutaneous injection of a glycerin extract of horse or dog adrenals. Since then organotherapy has been sufficiently tested to permit us to come to some conclusions in regard to its therapeutic value.

If we now inquire into therapeutic results they can be grouped under four headings, according to Gilbert and Carnot: (1) Adrenal therapy does harm—intolerance of medication, symptoms made worse, the fatal end hastened; (2) no effects are produced; (3) in some cases improvement is noted; (4) cure followed.

In Kinnicutt's list 6 cases out of 48 were cured, with improvement in 22 cases. Adams added 49 cases to this list, making 97 cases, of which

16 were cured and 31 were improved, and Sajous adds 23 to Adams' list, 120 cases in all then, of which 25 were cured and 36 improved. It will be seen that, in the short time in which organotherapy has been employed in this disease, the percentage of recoveries has increased from 12½ to 21, and improvement from 22 to 33 per cent. With all due allowance for errors in medical statistical research, we can certainly report good progress in the treatment of Addison's disease with adrenal therapy. The reasons for this are that early diagnosis is made more frequently, that milder cases are treated for what they are, and remedies are more efficacious.

As to the modus operandi of this treatment, all that can be said positively is that it does not act as organotherapy usually does in other diseases in which we have clinical pictures due to increase of or diminution in internal secretion, as in the thyroid gland. Boinet states that "it seems to act by causing a functional hyperactivity, reëstablishing the double action, pressor and antitoxic, of the portions of the capsule sufficiently healthy. Thus are explained the poor results in classic Addison's disease with its massive destruction of the adrenals. Its action is more favorable in the Addisonian syndrome, often secondary to pulmonary tuberculosis or any other antecedent infection, and in chronic adrenal insufficiency depending upon adrenal sclerosis, in that the cells are atrophic, degenerated but not completely destroyed." This view has been expressed by a number of authors. Moreover, it has been shown experimentally that adrenal tissue is very easily regenerated, so that this may help in the restitutio ad integrum, as has been shown by Poll.

Tuberculin.—Koch's tuberculin has also been employed. I know of no good results obtained from its use, and Billings has seen death occur in three patients within forty-eight hours of its administration. Iodid of potassium has been recommended here for the same indications. The principle of nil nocere must be followed in a disease in which a purge has been followed by a fatal issue.

Gland Transplantation.—As in the thyroid gland in permanent hypothyroidism, so in Addison's disease the transplantation of a healthy gland has been suggested (see Diseases of the Thyroid Gland). There is one great difference between hypothyroidism or anthyroidism and hypoadrenalism. In the absence of thyroids we can prevent damage or death by giving thyroid products with great certainty, not so in the absence of adrenals. We therefore are even more interested in the transplantation of the adrenals than in that of the thyroid gland. In lower animals transplantation has been successfully accomplished, and all the underlying principles necessary to success seem to have been worked out. Jabonlage was the first to transplant adrenals in the human being (1897). He transplanted fresh dogs' adrenal glands in two patients having Addison's disease; both died in twenty-four hours after the operation. As far as my literary

research goes, there are only eight transplantations on record in human beings, all of them ending fatally. There is no doubt that surgical methods and technic will overcome the present difficulties so that many of our patients with Addison's disease may be saved, as this seems the most promising treatment.

Therapeutic Measures.—Heretofore we have considered only the organotherapy of this disease, but it is necessary, in order to prolong life and to relieve and prevent suffering, to look to many other therapeutic measures. In the cases due to syphilis active antisyphilitic medication is demanded. From the standpoint of symptomatic treatment the principal therapeutic aim is to relieve adynamia. For this purpose the strength of the patient should be preserved by keeping him in bed, and this should be ordered even before the adynamia makes it necessary. The food is difficult of selection: it must be nutritious, it must be digestible, it must be appetizing, it must not be laxative. It is always best in this disease to consult the patient before laying down absolute dietetic laws. Progressive adynamia is to be feared very much; to prevent this it is necessary to make compromises, always selecting those articles of food and combinations of food which are the patient's choice, the object of this being to keep up and stimulate the patient's appetite. It is not an uncommon occurrence to have the anorexia so great that feeding is practically impossible. Even at best, the question of dieting is a difficult one, and as the disease progresses it grows more and more so. Various remedies have been recommended: iron preparations, arsenic, strychnia, nux vomica. Of these arsenic may be given in ascending doses until large ones are taken. I have seen good results follow its administration; remissions in two cases. Nux vomica is preferable to strychnia, as its effects upon the stomach are more marked and its local action is greater. Iron may be valuable for the anemia, and in this disease should be given as an organic iron compound. Alcohol is very valuable in asthenia; malt liquors, wines, whisky or brandy should be chosen according to their individual indications.

The gastro-intestinal symptoms require great attention. As a rule the stomach is deficient in gastric juice, both qualitatively and quantitatively (see Achylia). Nausea, vomiting, and pain must be treated. For the dyspepsia strychnia and diluted nitrohydrochloric acid may be given.

℞ Strychniæ sulphatis 0.03 gm.; gr. ss
Acidi nitrohydrochloridi diluti 15.00 c.c.; ℥ss
Six (6) drops in water after meals.

This dose should be gradually increased to ten drops or more three times daily. When the adynamia is present, diarrhea should be treated by dieting and bismuth preparations, tannic acid compounds, if necessary by opiates. Opium and morphia need not be given in very large doses for

checking diarrhea in this disease, the average dose being sufficient. The presence of intestinal auto-intoxication must always be considered.

Nervous Symptoms.—The nervous symptoms require attention. The psychic changes, which are not uncommon, lack of memory, mental sluggishness, or exaltation, cannot be controlled easily. General treatment, possibly in the direction of removing toxins in the blood, may be of value. Indeed this should be considered in connection with all the nervous symptoms: insomnia, tinnitus aurium, headache and faintness, stupor, and syncope. Moreover, the usual medication which gives relief for symptoms should be applied. Convulsions should be treated as a symptom.

The Circulatory Apparatus.—It is thoroughly understood that blood-pressure is low in Addison's disease; it would have been unnatural if, therefore, a routine treatment with vasoconstrictors had not been recommended. Epinephrin at least is no longer used, as it has proved unsatisfactory as a routine method. It is still recommended in cardiac asthma and should always be tried in the cardiac collapse which so frequently marks the beginning of the end. It should be given frequently and in combination with other vasoconstrictors, caffein especially, and with cardiac stimulants, ether, camphor, alcohol.

When authors are mentioned whose names are not in the list which follows, they can be found in the literature collected by Biedl in his excellent work on *Die innere Sekretion,* 1910.

Adrenal Hemorrhage.—Aside from the cases due to trauma, adrenal hemorrhage occurs spontaneously, in association with infections or as a result of thrombosis of the adrenal veins. Many of the apparently spontaneous cases occur in infancy or early childhood.

The symptoms associated with adrenal apoplexy, as it is sometimes called, may be of several types. The more important are as follows: The so-called peritoneal type in which there suddenly appear epigastric pain and tenderness, vomiting and profound prostration. The asthenic type in which profound weakness with death in a few days is the characteristic. The nervous type characterized by delirium, convulsions or coma, or a typhoid state. Cases in childhood are associated with purpura

Occasionally a definite tumor in the upper kidney region may be felt.

Treatment.—The diagnosis is so difficult that treatment is almost an academic question. The administration of adrenalin has been suggested by Bronselt.

Adrenal Insufficiency.—This condition is mentioned because it has so frequently been referred to in the literature of late. The clinical conception of adrenal insufficiency is based on such flimsy evidence and such gross misconceptions of adrenal physiology that no suggestions as to treatment are desirable.

Adrenal Tumors.—The position of the adrenal makes the early diagnosis of adrenal tumor almost impossible and the fact that nearly all

adrenal tumors are malignant and metastasize early makes the question of treatment of academic rather than practical interest. If the diagnosis of adrenal tumor can be made before signs of metastasis are evident, surgical removal is, of course, indicated.

REFERENCES

Aubertin and Bordet. Centralbl. f. innere Med., xxx, 976, 1909.
Baker, A. F. Ophthalmology, Jan., 1909.
Banti. The Treatment of Banti's Disease, Folia hæmatol., x, 33, 1910.
Boinet. Opotherapie Surrenale, Bull. acad. de méd., lxxii, 240, 1909.
Bramann. Deutsche med. Wchnschr., xxxv, 1738, 1909.
Buckley. Boston Med. & Surg. Journ., Nov. 7, 1907.
Dreyfus. Centralbl. d. ges. Therap., Nov. 23, 1905.
Eppinger, Falta, and Rüdinger. Ztschr. f. klin. Med., lxiii, 1908.
Eysselt. Wien. med. Wchnschr., lx, 394, 1910.
Falta. Zeitschrift. f. klin. Med., 1910.
Friedlander, A. Arch. Pediat., July, 1907. Ibid. 1911.
Gouget. Presse méd., 709, 1911.
Guer le Grand. The Present Status of the Treatment of Goiter, Old Dominion Journ. Med. & S., ix, 230, 1909.
Heinrich. München med. Wchnschr., 601, 1903.
Hunt, Reid and Atherton, Seidell. Bull. 47, Hygienic Laboratory Dep., U. S., 1909.
Jackson and Mead. Boston Med. & Surg. Journ., clviii, 346, 1908.
Jacobi, A. Diseases of Children, Mod. Clin. Med., 37.
Klose. Strassb. med. Zt., ii, 333, 1910.
Kuh, Sidney. Journ. Am. Med. Ass., xxxvii, 295.
Lenormant. Journ. de chir., 60, 1909.
Mayer. Arch. f. Gynaek, xc, 600, 1910.
Melchior. Berl. klin. Wchnschr., xlviii, 32, Aug. 7, 1911.
Möbius, P. J. Die Basedowsche Krankheit, 1906.
Moffitt, H. C. Tetany in Adults, Journ. Am. Med. Ass., lvii, 542, 1911.
Pfahler. N. Y. Med. Journ., 781, 1908.
Rehn. Deutsche med. Wchnschr., 1905.
Rogers. Ann. Surg., li, 145, 1910.
Sajous. Monthly Cycl. & Med. Bull., 228, 1909.
Sergent, E. Presse méd., xviii, 489, 1909.
Shattuck, F. C. Boston Med. & Surg. Journ., June 30, 1904.
Thomson, W. H. Am. Journ. Med. Sc., Dec., 1906.
Warthin. Arch. Pediat., xxvi, 579, 1909.
Wilms, M. Experiment. Erzeugung u. Ursach. d. Kropfes, Deutsche med. Wchnschr., xxxvi, 604, 1910.

CHAPTER XI

DISEASES OF THE THYROID GLAND

David Marine and Ernst P. Boas

Embryology, Anatomy and Developmental Defects.—The thyroid gland arises from a single median ventral tubular down-growth of the pharyngeal endoderm in or slightly anterior to the first aortic arch and anterior to the primitive lung tube. This down-growth divides into right and left halves and resembles an inverted T. The vertical arm or thyroglossal tract normally begins to undergo absorption about the sixth week of intra-uterine life but in districts where simple goiter is common the tract frequently persists as the pyramidal process or median lobe. When present, this tract is readily palpable as a smaller or larger pencil-like cord near the midline and extending upward from the thyroid isthmus. The presence of the thyroglossal tract after birth is therefore definite evidence of thyroid hypertrophy occurring during fetal life.

The normal adult human thyroid weighs between 20 and 30 gm. and does not exceed 0.35 gm. per kilo of body weight. It is shaped roughly like a horseshoe. The lateral lobes, usually about 5 cm. in length, are closely adapted to the lateral walls of the larynx and the angle between the larynx and the esophagus. The isthmus normally is a flattened band of thyroid tissue from 1 to 2 cm. in width and from 0.5 to 1 cm. in thickness connecting the two lateral lobes across the trachea anteriorly at the level of the second and third tracheal rings. The isthmus is the only portion of the normal thyroid that is palpable and this fact is of clinical importance in differentiating the normal thyroid from the milder grades of enlargement.

The more important developmental defects center about the down-growth and fate of the thyroid tract. Clinically, thyroglossal cysts and accessory thyroid tissue—the so-called lingual, sublingual, suprahyoid and infrahyoid thyroids—are the more important. Occasionally the descent of the thyroid tract is arrested and the entire mass remains above the hyoid bone—so-called lingual thyroids, enlargements of which have necessitated operation for obstruction. Unfortunately, such cases have been

operated on without first determining the presence or absence of thyroid tissue in the normal location.

Physiology.—The thyroid gland provides a means through its iodin-containing hormone for maintaining a higher rate of metabolism than would otherwise exist, and for varying this rate. Removal of the thyroid causes a decrease of as much as 40 per cent in heat production, and feeding thyroid causes a notable increase. These influences of the thyroid on metabolism were discovered in 1895 by Magnus-Levy. In 1895, Baumann discovered that iodin was a normal constituent of the thyroid and subsequent work has established the fact that the thyroid exerts its influence on metabolism by means of a very stable iodin-containing hormone which Kendall in 1916 isolated in crystalline form. This hormone is the only known active substance in the gland and is stored there in varying amounts. Measured as iodin, the maximum normal store is between 25 and 30 mg. or approximately 1 mg. per gram of fresh gland. Feeding iodin causes a rapid increase in the store to the maximum mentioned above. Iodin is present in the gland both in an active and inactive form. There is no fixed ratio between these forms, which shows that the active hormone is slowly and more or less continuously elaborated from the inactive iodin taken up from the blood-stream. All the evidence indicates that the activity of the thyroid is regulated chemically, mainly through the blood stream but also indirectly through its sympathetic nervous mechanism. The mechanism by which the thyroid hormone exerts its influence on metabolism is not understood. Sufficient, however, is known to indicate that this action is to a large extent determined or regulated by the interaction of other internal secretions as, for example, the augmentary action of epinephrin.

INFLAMMATION

(*Thyroiditis, Strumitis*)

The infectious theory of goiter gave rise to the view that all enlargements of the thyroid were chronic inflammatory reactions. There is no basis for this view. True inflammatory reactions are rare. So far as known they are never primary. Many of the so-called forms of *acute thyroiditis* or *thyroiditis simplex* are in truth only active hyperemias and cloudy swellings, manifestations of increased functional activity. Hyperemia and cloudy swelling usually accompany acute infections as part of the systemic or febrile reaction. They are seen also in food intoxications, drug and serum reactions and skin burns. Thyroiditis due to the administration of iodin has been described. This is erroneous. The administration of iodin to cases with goiter often causes the thyroid to become firm, even tem-

porarily enlarged and painful, due to the rapid accumulation of colloid in the alveoli. It comes on during the first week or two of iodin administration and subsides spontaneously.

Suppurative thyroiditis may occur in the course of puerperal infections, ulcerative endocarditis, scarlet fever, typhoid fever, influenza, pneumonia, tonsillitis, erysipelas, or as a direct extension from adjacent structures. It is more frequently seen in goiterous thyroids, especially in those with adenomas. Thyroid tissue with impaired vitality, particularly degenerating adenomas, form excellent foci for the lodgment and growth of pyogenic organisms. Injuries, as produced by the old iron and iodin injections or following the use of the seton, were frequently followed by necrosis and abscess formation. Primary tuberculosis of the thyroid is unknown but the thyroid is usually involved in generalized tuberculosis. In early pulmonary tuberculosis and in the secondary stage of syphilis the thyroid usually undergoes some enlargement. This hypertrophy is a part of the systemic reaction to these infections. Gummata of the thyroid have been observed. Riedel's struma is a rare form of chronic diffuse thyroiditis with lymphoid infiltration. Its etiology is unknown. Clinically this disease is usually mistaken for cancer.

The suppurative processes must be incised and drained. Other forms of thyroiditis require treatment only as part of the general diseases with which they are associated. Operative treatment of Riedel's struma should be limited to division, or at most excision, of the isthmus.

SIMPLE GOITER (STRUMA)

(*Endemic, Sporadic and Epidemic*)

Definition.—Simple goiter is a compensatory hypertrophy of the thyroid gland developing during the course of metabolic disturbances of unknown nature but depending immediately on a relative or absolute deficiency of iodin.

Distribution.—Simple goiter occurs sporadically and endemically in all animals having the ductless thyroid. While it may occur in any part of the world, in general, seacoasts are relatively free from the affection. In certain districts the incidence of thyroid enlargement is notably increased, the so-called endemic goiter districts. The most notable of these districts are the Great Lakes region and the Cascade Mountain district in North America, the Andes region in South America, the Alps in Europe and the Himalaya Mountain regions of Northern India. Occasionally sudden outbreaks of goiter have been observed in military garrisons, in fish hatcheries, in dairy herds, and on poultry farms, the so-called epidemic goiter.

Etiology.—The essential cause of simple goiter is unknown. The immediate cause is a relative or absolute lack of iodin. Goiter is, therefore, only a local sign or effect of a specific deficiency disease and may result from any factor (*a*) which increases the iodin needs of the organism as during puberty, pregnancy and lactation, or during certain infectious diseases; (*b*) which interferes with the normal absorption and utilization of iodin, as in partial removal of the thyroid; or (*c*) from the actual experimental deprivation of iodin. Drinking water has been associated with the etiology from the earliest times but we still do not know the nature of the association. A great variety of chemical substances have been put forward as causative agents but none has been shown to have any definite relation. Likewise bacteria have been considered as etiologic factors but the general belief to-day is that living viruses play only a secondary or indirect rôle.

Simple goiter may be congenital or acquired. The acquired form is seen most frequently around the age of puberty, during pregnancy and lactation and during the menopause.

Pathological Anatomy.—A wide range of morphological changes may be present, depending on the duration of the enlargement and on the species of animal. The enlargement begins with hyperemia, a decrease in the colloid and an hypertrophy and hyperplasia of the alveolar epithelium. From its developmental or actively hyperplastic stage, the gland may involute to the colloid or quiescent or resting stage, or the hyperplasia may go on to exhaustion atrophy. Simple goiters, as seen surgically, are usually in the resting stage, the so-called colloid or cystic goiters of the older writers. In man, the thyroid hyperplasia is frequently irregular and nodular. The nodular form is designated struma nodosa in Europe and adenomatous goiter in America. These nodules or adenomata are believed to be due to different rates of growth of foci of cells of different physiologic age. These foci have been designated by Woeffler as fetal rests. The stimulus which initiates the growth of the more differentiated thyroid tissue and that which initiates the growth of the cell rest are probably identical. These nodular growths have certain of the attributes of tumor in that their growth may not be arrested by iodin or by natural physiological recovery. On the other hand, many of these so-called adenomata are capable of functioning, and it is not possible to distinguish the functionally active from the functionally inactive by morphological studies.

In long-standing goiters a great variety of terminal metamorphoses may be present. Among the more common of these secondary changes are hemorrhage, cyst formation and calcification. Adenomata are more frequently the seat of these changes and, in addition, they are the basis of at least 90 per cent of thyroid carcinomas.

Pathological Physiology.—Thyroid enlargement is primarily a work hypertrophy in response to a physiological deficiency. There are all

degrees of this insufficiency. In the milder grades no physiological manifestations are detectable, while in the severe degrees myxedema and cretinism result. The pathological physiology of simple goiter may be expressed most briefly in Morel's dictum, "Goiter is the first step toward cretinism." The first change in the thyroid in developing goiter is a marked decrease in the iodin store. It long antedates the morphological changes. The average normal iodin store is about 0.2 per cent of the dried gland. It has been shown experimentally that if the iodin store is maintained above 0.1 per cent no hypertrophic change can occur. As the iodin store decreases below 0.1 per cent the hypertrophic and hyperplastic changes progressively increase so that in the extreme degrees of hyperplasia iodin is either absent or present only in traces. Such hyperplastic tissue has an extraordinary affinity for taking iodin from the blood-stream.

General Treatment.—The therapy of simple goiter may be divided into two parts, (1) its prevention, and (2) its treatment.

Preventive Treatment.—Simple goiter is the easiest and cheapest of all known diseases to prevent both in man and in animals. The principle of its prevention depends on the facts that if the iodin store in the gland is constantly maintained above 0.1 per cent, no enlargement can occur, and secondly, that the maximum storage in the normal adult human thyroid is around 20 to 25 mg. Iodin in any form and administered in any manner is effective. This fact introduces difficulties and advantages, difficulties regarding the selection of the best form and manner of administration, and advantages in that the desired result may be accomplished with certainty in a great variety of ways. The ideal plan of administration of iodin in goiter prevention is still to be worked out.

In private practice, 30 c.c. of syrup of hydriodic acid given in ½ to 1 c.c. doses daily, and repeated each spring and autumn, is sufficient. In Switzerland, iodostarin tablets containing from 1 to 5 mg. of iodin have been given at weekly intervals throughout the year. In endemic goiter districts where it is necessary to protect the whole or large fractions of the population, prevention should be made a public health measure. In applying prevention to the school population, Marine and Kimball have found sodium iodid convenient and effective. Two gm. of sodium iodid were given in 0.3-gm. doses daily and repeated each autumn and spring. One gm. distributed over a period of a month and repeated twice yearly is equally efficacious. If the entire population is to be protected, iodized table salt would seem to be the most practical preparation. For this purpose, ordinary sea salt if used exclusively, or a salt containing from 1.0 to 2.0 mg. per kilo. if restricted to table use, would seem ample. The protection against thyroid hypertrophy in the mother during pregnancy and lactation, and in the fetus, may be obtained by the administration of 30 c.c. of syrup of hydriodic acid or of an equal amount of iodin in any other suitable form extending over a month during the first half of pregnancy.

With the increasing public demand for medical supervision of women during pregnancy, the prevention of goiter in both mother and fetus could be made a routine public health measure in goiter districts.

While theoretically desiccated thyroid is a more specific prophylactic measure than iodin, practically it is too dangerous a drug to be recommended for this purpose. Other means of prevention have been advocated, the most important of which is changing the water supply. This has been carried out with some success in a few places but obviously its application is very limited and we believe unwarranted.

Dangers and Untoward Effects.—The use of iodin in the amounts above recommended for the prevention of goiter is not associated with any noteworthy dangers. Occasionally, iodism may be observed and it is possible, though improbable, that in highly susceptible individuals exophthalmic goiter may be initiated, or that cases of early Graves' disease may be aggravated by the administration even of these small amounts of iodin. In general iodin should not be administered when the suggestion of Graves' disease is present, although it is well known that many cases of Graves' disease may be benefited by the daily administration of iodin in milligram doses. It is certain that the dangers of initiating Graves' disease by the use of iodin have been exaggerated and most, if not all, instances have been due to the gross abuse of iodin or desiccated thyroid alone or combined.

Curative Treatment—*Medical.*—In well-advanced long-standing cases of goiter no plan of medical treatment is satisfactory. In the early developmental stages of goiter, the curative effects of iodin in doses recommended under Prevention, or even of desiccated thyroid, are most striking, and bring about complete relief in the majority of such cases if not complicated by adenoma, cyst, hemorrhage, etc.

The most satisfactory plan of treatment is as follows: Give 2 to 4 gm. of desiccated thyroid in 0.2 gm. doses daily, then allow a two weeks' interval of rest and saturate the gland with iodin, by giving 30 c.c. of syrup of hydriodic acid or its equivalent in any other practical form in 1 to 2 c.c. doses daily. This treatment may be repeated every third or sixth month. No further benefit need be expected from larger amounts or more frequent administration. These amounts of iodin and desiccated thyroid quickly relieve the physiological insufficiency but the involution or regression of the goiter requires several months. The maximum reduction in the size of the simple goiter will occur in from six to twelve months. The external application of iodin should be condemned. True adenomata are not affected by the administration of iodin and surgical removal offers the only certain means of relief. Indirect measures, depending on the etiological factors involved, such as the removal of adenoids and tonsils, the institution of antisyphilitic treatment or appropriate gynecological operations should be carried out where necessary. Roentgen rays and radium are of little practical value and may produce adhesions which

make operative procedures more difficult. Again, the dangers to be looked for in the treatment of goiter by iodin and desiccated thyroid are iodism and exophthalmic goiter. Iodism is a negligible factor. On the other hand, exophthalmic goiter is more important because patients with goiter are usually of the age at which exophthalmic goiter most frequently develops. In general, neither iodin nor desiccated thyroid should be administered to individuals in whom Graves' disease is suspected unless the patient is under hospital control. The danger of desiccated thyroid lies in the fact that many apparently normal individuals are abnormally sensitive to it. However, when one considers the almost universal use of iodin in one form or another, and in doses far above those necessary for optimum thyroid effects, it becomes obvious that dangers from the amounts of thyroid or iodin in the doses indicated for treatment are of minor importance.

Surgical.—In our opinion all simple goiters should be iodized before operation as described above. This makes the gland firmer, easier to handle, involutes any existing hyperplasia and reduces the vascularity. An operation should be considered where medical treatment fails to bring about sufficient reduction, when adenomata are present, for the relief of pressure effects and deformity. Adenomata can be treated successfully only by removal and on account of the serious terminal metamorphoses which they may undergo, for example, cyst formation, hemorrhage and malignant tumors, they should be referred to the surgeon.

MYXEDEMA

Myxedema is a chronic disease due to a high-grade thyroid insufficiency and characterized by a greatly reduced metabolism resulting in stunted mental and physical development if occurring during the growing period, and in trophic disturbances, cachexia, and mental deterioration if occurring in adults. Even the severest forms of myxedema usually have some functioning thyroid and there are all gradations of the disease from the severest form down to and below the threshold of clinical detectability.

Clinically, the disease may be arbitrarily divided into two groups, depending on whether it develops before or after puberty: (1) congenital and infantile myxedema (cretinism); (2) adult myxedema (spontaneous Gull's disease, and operative).

Congenital and Infantile Myxedema (Cretinism)

Occurrence.—The disease occurs sporadically and endemically. The sporadic form is rare and may occur anywhere, while the endemic form is intimately associated with endemic goiter both geographically and etiologically. The incidence of endemic myxedema varies with the

severity of the goiter district. Infantile myxedema is also called cretinism. Many observers believe that cretinism is a much more complex nutritional disturbance than can be accounted for on the basis of thyroid insufficiency alone. This belief is due to the fact that many other conditions have been confused with cretinism and that postnatal treatment with desiccated thyroid in well-developed cases is usually only partially successful. The most rapid bodily development takes place during fetal life and the greatest effects of thyroid insufficiency also occur during this period. A more physiological test would be to give thyroid or iodin to the mother during pregnancy. The question is raised because of the ease with which congenital myxedema or cretinism in animals may be controlled by the administration of iodin or thyroid during pregnancy. On the basis, therefore, of the experimental work, it is believed that all of the essential changes in cretinism may be directly or indirectly ascribed to a thyroid insufficiency. Dwarfism, rickets, Mongolian idiocy and pituitary deficiencies are the diseases most commonly confused with cretinism and are still included under this category by many observers. Cretinism is from two to three times more common in females, though the statistics are very unreliable.

Etiology.—We believe that the causes of endemic myxedema and of endemic goiter are essentially identical. Both are functional insufficiencies of the thyroid. Goiter is the first sign of a functional insufficiency of the thyroid, and myxedema is the end stage of the severest form of this insufficiency. A recognizable degree of cretinism may appear in the first generation of goiterous parents, but usually it is a summation of several generations of progressively increasing thyroid insufficiency. Only the milder grades of cretins are fertile or capable of producing viable offspring.

In animals a recognizable myxedema may appear in one generation, but usually it also appears after several generations of increasing thyroid insufficiency. A loss of thyroid function sufficient to cause recognizable myxedema may be due to a great variety of causes. Thus, injury or destruction of the gland by infection or trauma, congenital absence or smallness of the thyroid anlage, or atrophy of unknown nature, are the most common causes of sporadic infantile myxedema, while endemic goiter is the most important additional factor in endemic myxedema.

Pathology.—Essentially identical tissue changes occur in both the endemic and sporadic forms. The skeleton is dwarfed and deformed. This is due to a partial suppression of growth and not to a specific interference with the processes of bone formation as in the case of rickets. Rickets is an independent disease. In myxedema there is both decreased formation of osteoid tissue and decreased ossification. The degree of the bony changes depends on the age at which the disease begins and on the degree of thyroid insufficiency. Remarkable growth of the skeleton may

occur following the use of desiccated thyroid if begun before the capacity for growth is lost, which in this disease is much later in life than normally.

The thymus often persists. The spleen and lymphoid tissues throughout the body are slightly enlarged. There is a lymphocytosis. The anterior lobe of the pituitary is often enlarged. The thyroid gland may be absent, markedly reduced in size, or, as occurs in the majority of cases of endemic cretinism, greatly enlarged. This enlargement in the earlier developmental stages consists of an active hyperplasia, which later gives way to exhaustion atrophy and sclerosis. The alveoli of such hypertrophic sclerosed glands are reduced to nests of irregular cells. Sometimes follicles distended with colloid and lined with flattened epithelial cells are scattered throughout the sclerotic mass. Well preserved multiple adenomata are usually present in the goiterous thyroids.

Pathological Physiology.—The essential physiological fault is a loss of the iodin-containing hormone sufficient to inhibit growth and development. The cretins seen in the clinic are only partial cretins, as the severest cases, both in animals and man, die soon after birth. In adult animals there may be complete absence of the thyroid function with the preservation of vegetative life for years. All the symptoms to be enumerated may be explained on the inability of the organ to maintain the level of metabolism which insures normal nutrition, growth and development.

Symptoms.—These are identical in both the sporadic and endemic forms. There are all degrees of severity of the symptoms above the threshold of clinical detectability. The disease may be arbitrarily divided as follows: congenital cretinism, late infantile cretinism, and the juvenile forms resembling and overlapping myxedema of adults. In the severer forms of congenital cretinism both in man and animals, the body has the appearance of generalized edema. Body weight is usually somewhat increased. Such cases rarely survive. The milder forms are usually recognizable clinically between the sixth month and the second year. The child has a waxy appearance, the tongue is large, the face expressionless, muscular movements sluggish, the abdomen protrudes, and deafness and inability to talk may be noted. The hair and nails are dry and brittle and teething is delayed and irregular. In the endemic form the thyroid gland is usually enlarged. In older children, growth and development, both physical and mental, seem at a standstill. Of all the manifold manifestations of the disease, the decreased heat production is the only specific test and, with the increasing use of apparatus for measuring heat production, all suspected cases should be subjected to this test. Infantile myxedema may be confused with dwarfism, Mongolian idiocy, rickets, achondroplasia, congenital adiposity, osteogenesis imperfecta and scleroderma. The only certain differentiation in atypical cases is by means of heat production measurements.

Prophylaxis.—Prevention is the plan of choice and should be carried out routinely in endemic goiter districts, since the available evidence indicates that endemic cretinism is due to the same physiological fault as endemic goiter. It has been clearly established that congenital myxedema in animals is readily controlled by the administration of iodin to the mother during pregnancy. We believe the elimination of endemic cretinism is as simple as the elimination of endemic goiter and can be accomplished by the same means. To this end it is necessary to see that the mother obtains 2 to 5 mg. of iodin weekly in some available form during pregnancy and lactation, and that similar amounts of iodin be continued throughout the growing period of the child. The most practical means of carrying out this treatment is the state-wide use of iodized salt, that is, salt containing from 1 to 2 mg. of iodin per kilo. In addition to the specific prophylaxis, the food should be sufficiently varied to insure the presence of the other elements necessary for nutrition. Improvement in the hygienic conditions and, in certain regions, changing the water supply have been important factors. With sporadic cretinism no general prophylaxis is possible.

Treatment.—*Iodin and Thyroid.*—The milder forms of endemic infantile myxedema, if recognized very early and while there is still plenty of active thyroid tissue, can be cured by the use of 2 to 5 mg. of iodin daily. If the gland has undergone exhaustion atrophy, desiccated thyroid is necessary. Infants and children withstand relatively larger doses of desiccated thyroid than do adults. It is better to start with 0.1 gm. of desiccated thyroid three times daily and increase or decrease this dose according to the indications. After a month, this dose can usually be much reduced and there is no physiological reason why a larger dose once a week would not suffice. As already pointed out, when there is plenty of active thyroid, iodin is as efficacious as desiccated thyroid, but even where the thyroid is atrophic it is well to include small doses of iodin intermittently with the desiccated thyroid. Thyroxin has no advantages over desiccated thyroid and many disadvantages. The ideal control of dosage is by means of heat production measurements. In the absence of this, the optimum permanent dose can be found only by more prolonged experimentation. There is no physiological basis for doses of desiccated thyroid larger than those indicated, although there are recorded instances in which 5 gm. of desiccated thyroid have been given daily. Such doses of standardized thyroid are dangerous and should never be used. Thyroid homotransplants are rapidly destroyed by the host and are therefore valueless.

General Measures.—The diet should be full with possibly a restriction of fats. Fresh air, exercise, both mental and physical, and other elements incident to normal child life should be provided. In other words, all of the general hygiene and educational measures ordinarily used in the treatment of an underdeveloped child should be employed.

Myxedema of Adults (Spontaneous, Gull's Disease, Operative)

Etiology.—Myxedema in adults is the best understood effect of a pathologic decrease in thyroid function because it is not complicated by the intricate and little understood processes of growth and development. Spontaneous and operative myxedema are essentially identical. Complete removal of the thyroid causes a drop in heat production up to 40 per cent of the normal. This fall begins about six to eight days after thyroidectomy in animals and presumably about the same time in man. Transient myxedema often follows partial thyroidectomy for goiter. Spontaneous myxedema is six to eight times more common in females and is closely associated with the menopause. Most of the cases occur in the fourth and fifth decades. Exophthalmic goiter is the most important forerunner of myxedema. Simple goiter appears to be protective. Any condition that creates a prolonged functional strain on the thyroid may lead to exhaustion atrophy. Rapid childbearing, certain infectious diseases, pelvic inflammatory disease, and prolonged psychic shocks appear to be exciting causes in certain cases.

Pathological Anatomy.—The thyroid gland is usually reduced in size and in some cases no thyroid tissue has been found. Enlargement of the thyroid may, however, be present, especially in goiter districts. Enlargement is usually due to the presence of adenomata since the more differentiated thyroid tissue has undergone complete fibrosis. In a typical case, the thyroid is withered and tough with no visible colloid, and microscopically the alveoli are compressed to small nests of irregular degenerating cells embedded in the fibrous tissue; occasionally masses of colloid may be seen. These are the remnants of previously enlarged colloid-filled follicles in which excretion was blocked. Von Eiselberg's case of myxedema relieved by the recurrence of a thyroid carcinoma may be doubted. There is a great deal of direct experimental evidnece that thyroid carcinoma is incapable of normal function.

There is usually a relative lymphocytosis and an enlargement of the spleen and lymph glands. In many cases the thymus is also present and shows active lymphoid tissue. The anterior lobe of the pituitary may be enlarged. The change in the corium and subcutaneous tissues, which led Ord to propose the name "myxedema" is described as a solid edema due to swelling of, and possibly an increase in the collagen material. No characteristic changes have been observed in the nervous system.

Symptoms.—These develop slowly over weeks or years and the sallow color and thickening and dryness of the skin, loss of hair, together with the gradual mental deterioration are often the most obvious symptoms. The pulse is slow, the blood-pressure is usually low, and a moderate secondary anemia is present. Symptoms referable to the nervous system are

sleeplessness, loss of memory, slow speech and clumsy and uncertain muscular movements. The temperature is often subnormal. The one characteristic manifestation is a great reduction in heat production. Heat production measurements should be made in all suspected cases. In the severest form it may be reduced 40 per cent, but usually the decrease ranges from 20 to 30 per cent. Glycosuria is rare and the alimentary sugar tolerance is usually increased. Albuminuria is more frequent and occasionally a high-grade nephritis may be present which offers the most important problem in differential diagnosis.

Prognosis.—Spontaneous recovery occurs only in cases with active thyroid tissue, as after partial thyroidectomy and in acute cases with enlarged actively hyperplastic goiters. In untreated cases the average duration of life is from five to seven years. With thyroid opotherapy it is possible to cure or control the disease.

Treatment.—In the rare cases in which there is abundant active thyroid tissue, iodin is as efficacious as desiccated thyroid. When the thyroid has undergone complete exhaustion atrophy, as is usual in Gull's disease, it is necessary to supply the preformed iodin-containing hormone. This is best administered as desiccated thyroid. Thyroxin has no advantages and many disadvantages. One may begin with 0.1 gm. of desiccated thyroid three times daily. Visible effects usually appear in about one week. Elevation of the pulse rate, body temperature, and a slight loss in weight are among the first signs. The dose may be increased to 0.2 gm. three times daily during the second week or reduced if not well tolerated. During the next two or three months it will be necessary to experiment with the dosage to determine the optimum amount for the particular case. This is best done by periodic measurements of heat production. After a symptomatic cure has been brought about it will be necessary to reduce the dose to approximately the daily requirements, which should not exceed 0.1 gm. daily. We know of no pharmacological reason why the permanent dose of desiccated thyroid should not be given once or twice weekly instead of daily. Certain cases, especially those following exophthalmic goiter, and those going through the menopause, must be more carefully watched even when smaller doses than above suggested are used.

GRAVES' DISEASE

Definition.—Graves' disease is the manifestation of a disturbance of the regulatory control and functional interaction of organ activities dependent upon an inherited or acquired constitutional anomaly and characterized by increased metabolism, asthenia, and tachycardia.

Prevalence.—Graves' disease occurs at all ages, but is most frequent in the third and fourth decades and at the time of the menopause.

Hereditary influences often establish a predisposition to the disease. Neuropathic disorders, vasomotor neuroses, status thymicolymphaticus, and simple goiter often occur in families of patients with exophthalmic goiter. Statistics indicate that the disease is from six to nine times more common in females. Race also is an apparent factor. Thus, exophthalmic goiter is rare in negroes. McCarrison observed few cases in India, even in regions where the entire population had simple goiter. Graves' disease is rare among the Chinese and Japanese. It has never been observed in animals.

Etiology.—The essential metabolic disturbance underlying Graves' disease is unknown. A great variety of factors apparently may act as exciting causes. A certain number of cases develop after acute mental or emotional anguish, but more frequently they follow protracted emotional disturbance and mental strain. The predisposing effect of certain occupations may thus be explained. In some cases, physical trauma seems to be the exciting agent.

Infectious diseases are important in the etiology. Of these, rheumatic fever, typhoid fever, influenza and syphilis are the most significant. The syphilitic infection may be either congenital or acquired. There is evidence that infections act in part at least by injuring the functional activity of the suprarenal cortex. Tuberculosis occupies a slightly different position from that of the other infectious diseases. Frank Graves' disease rarely develops, but an incomplete syndrome is found in from 10 to 25 per cent of patients in the earlier stages of tuberculosis.

The excessive administration of iodin or of desiccated thyroid to susceptible individuals may initiate the symptoms of Graves' disease. The extensive use of iodin and the relative infrequency of this sequel indicates that there must be a predisposing constitutional anomaly in these patients.

Facts pointing to the relation of the sex glands to Graves' disease are the frequent onset during the menopause, at puberty, in association with disturbances of menstruation, with pelvic diseases and the occasional development of symptoms during pregnancy.

Pathological Anatomy.—The changes are body-wide and one can at present only catalogue them in the order of their constancy and prominence. The thyroid gland, as pointed out by Virchow, may exhibit all the variations seen in other clinical diseases associated with goiter. Some degree of active hyperplasia is present in about 70 per cent. Adenomata, colloid goiters, and rarely carcinoma may be present. Occasionally the appearance of the gland may be normal. As pointed out by Marie, the thymus may regenerate. The spleen is usually moderately enlarged as are also the lymph-nodes and intra-organ lymphoid tissue, particularly in the thyroid, lung and liver. A variety of ill-defined lesions have been described in the nervous system. Miliary hemorrhages in the basal ganglia and atrophy and fibrosis of the restiform bodies have been noted. Pigmen-

tation and atrophy of the sympathetic ganglia have also been observed. The central nervous system is without doubt profoundly affected but, as Gowers pointed out, the changes involve the finer cell nutrition and cannot be detected by our present morphological methods. In the late stages fibrosis and round-cell infiltration occur in the cardiac muscle. The skeletal muscles may show fatty metamorphosis. The liver is usually somewhat reduced in size and often shows definite cirrhotic changes. The morphologic changes observed in the pituitary, suprarenals, ovaries and testes are inconstant.

Pathological Physiology.—Graves' disease is a highly complex disturbance of the regulatory control and functional interaction of many organ activities. Manifestations of decreased activity succeed manifestations of increased activity in the same organs and evidence of decreased activity of some tissues and of increased activity of others usually coexist. Interest centers around the thyroid gland. There is no doubt that hyperactivity of the thyroid determines the increase in heat production. This activity is exerted by means of its iodin-containing hormone. Epinephrin augments the action of the thyroid hormone and this fact is the basis of the Asher-Goetsch test. While it is probable that there is an increased discharge of epinephrin in Graves' disease it cannot be demonstrated. The thyroid-suprarenal cortex interrelationship is also disturbed. Recent work has shown that the suprarenal cortex exercises a regulatory or inhibitory action on the thyroid and it is probable that in Graves' disease there is a partial loss of this cortical control. The increased activity of the thyroid could be explained as due in part to the stimulating effect of an increased epinephrin excretion plus a decreased inhibitory control by the cortex. The nature of the hyperplasia of the lymphoid tissues is believed to be compensatory and secondary to injury of the suprarenal cortex and gonads. The alimentary hyperglycemia is believed to depend on an impairment of the glycogenic function of the liver. The relation of the cirrhotic changes in the liver to the decreased sugar tolerance is unknown. Some sex gland functions are often increased in the earlier stages of Graves' disease and more or less depressed in its later stages.

Symptomatology

For convenience of discussion, the Graves' syndrome may be divided into two main types, the complete or primary, and the incomplete or secondary. Graves' disease is chronic, progressive and cyclic in its course.

Complete Graves' Disease.—The classical symptoms, goiter, tachycardia, exophthalmos, and tremor, are not constant. Tachycardia is one of the earliest symptoms and is never lacking while the disease is active. The pulse rate is constantly high, ranging from 100 to 200 per minute. The constancy of the tachycardia differentiates Graves' disease from many

neuropathic and vasomotor disorders. The correlation between the heart rate and basal metabolism is close and within limits the pulse rate parallels the basal metabolic rate.

Asthenia is a very constant symptom. Myasthenia is general and can be demonstrated in all somatic muscles. The thyroid enlargement, while sometimes absent, is usually moderate, symmetrical, soft, vascular and pulsating. Loss of weight is usually striking and may be traced to the increased oxidation within the body. Magnus-Levy first observed the increased heat production but it is only within the last few years through the development of appropriate apparatus that measurements of heat production have become important in diagnosis. In general, the basal metabolic rate is the best available index of the severity of the disease. Occasionally the temperature is slightly elevated. Tremor is closely correlated with the degree of muscular weakness and is usually rapid and fine. It is increased by mental excitement and fatigue.

The importance of the eye signs has been exaggerated. Exophthalmos occurs in about one-third of all cases. Among the other ocular signs, the lagging of the upper lid when the patient is directed to look down, the widening of the palpebral fissure, infrequent winking and difficulty of convergence may be enumerated. Mental symptoms are usually in evidence. The patient is restless, irritable and excitable. Occasionally, acute mania or melancholia may supervene. Vasomotor disturbances and sweating may also be traced to disturbances of the nervous system. Gastrointestinal symptoms are common. The appetite is often increased, vomiting may occur, and gastric anacidity has been frequently observed. There is often increased motor activity of the intestinal tract giving rise to diarrhea. Alimentary hyperglycemia and glycosuria are found in about one-third of the cases. True diabetes, however, is rare.

Disorders of the cardiovascular system are among the most important symptoms of Graves' disease. Much has been written concerning the goiter heart but there is no clear concept of its underlying pathologic physiology. The goiter heart is present both in simple and in exophthalmic goiter, but in exophthalmic goiter there are additional myocardial disturbances. In simple goiter, cardiac hypertrophy is usually proportional to the size of the goiter. Marine has demonstrated this in animals and believes that the cardiac hypertrophy is primarily a work hypertrophy. In the later stages there is dilatation of the cardiac chambers, particularly of the right heart, possibly depending on an increased blood-pressure in the pulmonary circulation. Others believe that toxic influences of thyroid origin are the determining factors. Whatever the etiological factor the enlarged heart associated with simple goiter may become insufficient.

The heart in Graves' disease presents quite a different picture. In addition to the moderate hypertrophy and dilatation seen in the simple

goiter heart there may occur scars and round-cell infiltrations, evidences of some nutritional disturbance or deficiency, acting both through the blood-stream and the cardiac nerves. Patients complain of palpitation, pulsations in the neck as well as of shortness of breath. Physical examination reveals an overactive heart with a diffuse strong apex beat. The systolic blood-pressure is usually elevated while the diastolic pressure is normal or low. In certain cases the blood-pressure is low, particularly in patients with marked asthenia who are in the exhaustion stage of the disease. If the Graves' syndrome does not last too long the heart may be restored to normal, otherwise the cardiac involvement becomes more serious. At first extrasystoles may appear. Later auricular fibrillation occurs, at first paroxysmally, then continuously. Signs of myocardial insufficiency and stasis in the peripheral circulation then become manifest. Cardiac damage of this degree is usually not relieved by the arrest of the Graves' disease.

The leukopenia and lymphocytosis have been emphasized by Kocher. While a lymphocytosis is very common in Graves' disease and is probably associated with the general lymphoid hyperplasia, the hemoglobin and red cell count are usually normal.

Menstrual disturbances are common. In the earlier stages the frequency and amount of bleeding may be increased. In the later stages this function is diminished or absent. Pregnancy usually exerts a favorable effect on the course of the disease but is distinctly harmful when there are signs of organic cardiac disease. Lactation almost invariably aggravates the clinical picture of exophthalmic goiter.

Incomplete Graves' Disease.—This is a very difficult group for diagnosis. These cases are easily confused with other disorders such as neurocirculatory asthenia, vasomotor neuroses, menopause phenomena and early pulmonary tuberculosis.

No satisfactory classification of the incomplete forms of Graves' disease exists. Patients with many of the symptoms of Graves' disease, in whom certain of the common signs, particularly loss of weight, goiter, and eye signs may be lacking, and those with long-standing adenomatous goiters, belong to this group. On the average the patients are older than those presenting the complete Graves' syndrome. Most of the cases occur in the fifth decade and in them the disease is often associated with long standing goiter or with menopause phenomena. It is the incomplete forms which have contributed chiefly to the confusion and lack of clearness in the clinical picture of Graves' disease, particularly in the discussion of its treatment. The diagnosis of incomplete Graves' disease should at present be restricted to patients who exhibit persistent tachycardia, asthenia and an increase in their basal metabolic rate. The other symptoms vary greatly in their incidence and severity. Cardiovascular signs and symptoms are usually prominent. Mental symptoms, vasomotor disorders

and excessive sweating are common. Tremor is present in about one-half the cases. Diarrhea and great loss of weight are rarely seen.

Diagnostic Criteria.—Frank cases of Graves' disease offer no difficulties in diagnosis. The essential signs are constant tachycardia, asthenia, loss in weight and tremor. Diarrhea, goiter, and eye signs when present complete the clinical picture. Of laboratory procedures, the determination of the basal metabolic rate is one of the most valuable aids in the diagnosis, though in certain cases of evident Graves' disease this may be normal or even subnormal at the time of examination. The test for alimentary hyperglycemia is of value. While patients with Graves' disease are hypersensitive to epinephrin many observers have shown that hypersensitiveness occurs in other conditions and in apparently normal individuals. In severe cases of Graves' disease, the injection of 0.5 mg. of epinephrin is dangerous.

Course of the Disease.—Graves' disease is essentially chronic in its course. It is marked by remissions and exacerbations which may extend over periods of several years. Cases occur which run their course to death or recovery within a month. The longer the duration of the disease the more do the cardiovascular symptoms, particularly signs of myocardial insufficiency, dominate the clinical picture. Symptoms of myxedema occasionally supervene in the course of the disease as do also manifestations of Addison's disease.

Prognosis.—The outlook for partial recovery is good. Complete restoration to health is unusual. The prognosis in the individual case depends on the mode of onset, the duration of the symptoms, their severity, the damage which has been suffered by the heart, and on the economic position of the patient. Some cases of sudden onset completely recover. Some progress rapidly to a fatal outcome but most of them pass into the chronic stage. The longer the symptoms have lasted the poorer is the outlook for complete recovery. If the heart shows evidence of organic disease the outcome in most instances is cardiac failure.

Prophylaxis.—A proper prophylaxis of the disease is difficult because there is no single known etiologic agent concerned in its production. It is well to remember that excessive administration of iodin or of desiccated thyroid in predisposed individuals may provoke the disease. Because of the close relationship of exophthalmic goiter with puberty, menopause and pregnancy, as well as with many acute infectious diseases, the physician should be alert for the first signs of the disease. It is important for physicians in charge of industries employing women, and for those who come in contact with school teachers, to watch for the early signs of the disease. The children of mothers with active Graves' disease usually are born with simple goiter. This can and should be prevented by the administration of 15 c.c. of syrup of hydriodic acid in 1 c.c. doses daily during the first half of pregnancy.

Treatment

There is as yet no unanimity of opinion whether medical or surgical treatment in Graves' disease is the better. We are of the opinion that with rare exceptions medical treatment should be given a thorough trial before surgical procedures are instituted.

General Measures.—The prime requisite is to provide physical and mental rest. Any form of rest cure in which no allowance is made for the nervous instability and emotionalism of these patients is bound to fail. The personality of the physician is often of more importance than the measures which he may employ. Indeed, it is evident from a survey of the many different therapeutic procedures employed in the treatment of Graves' disease that it was the personality of the physician rather than the remedies used that was of benefit. The strictness and duration of the rest treatment will depend on the severity of the disease. Patients should be confined to bed for at least two weeks. Rest in bed, however, is ineffectual unless the causes of the mental and emotional disturbances are removed. To accomplish this it is necessary to remove the patient from his natural environment and familial associations. Such complete rest and isolation should be continued for a variable time, depending on the lessening of the symptoms. The chief clinical guides to improvement are the pulse rate, basal metabolism, and a gain in weight and strength.

It is at once apparent that the ideal methods just described are available only to wealthier patients. For the others, the problem is much more difficult and the ingenuity of the physician will be taxed to obtain the most favorable conditions for the patient. As close an approximation to the ideal as possible should be obtained. Treatment in the general wards of a hospital is usually unsatisfactory. In mild cases complete rest may be unnecessary. Whenever possible they should give up for a time their present occupation and should be relieved of all their responsibilities. Depending on the case certain rest hours during the day should be prescribed and hours of sleep should be defined. Detailed instructions as to the apportionment of the patient's time should be given. A vacation in the country or a visit with congenial friends may greatly benefit a mild case.

Hydrotherapy may be used as a general measure and for the relief of individual symptoms. A bath at a temperature of 95° F. for about fifteen minutes is often restful and particularly useful in combating insomnia. The more vigorous forms of hydrotherapy are contra-indicated. If there is much swelling and pulsation of the thyroid gland or palpitation of the heart, an ice-coil or ice-bag over the thyroid and heart will be found useful. The bowels should be kept open, preferably by means of a mild saline purge such as sodium phosphate.

Diet.—In the absence of severe gastro-intestinal complications the diet should be a mixed one and liberal. It must be borne in mind that the increased oxidation in the body demands more food. The patient's weight, which should be taken at least twice a week, is a good index of the adequacy of the diet. It is often advisable to prescribe five or six meals in the course of the day. The protein and fat intake should be somewhat restricted. Stimulants should be avoided.[1]

Focal Infections.—Although one cannot expect radical cures following the removal of foci of infection, it is rational to suppose that the continuous absorption of toxins may aggravate the disease. Infections should be sought for particularly in the tonsils and in the teeth. If the tonsils are definitely diseased, or if the patient gives a history of repeated attacks of tonsillitis, it is well to remove the tonsils if the general condition of the patient warrants. A number of cases show considerable improvement following this measure. Simple hypertrophy of the tonsils is a common finding in Graves' disease and does not justify their removal. Teeth should be extracted only when there is conclusive evidence of root infection. Diseases of the accessory nasal sinuses, of the gall-bladder, of the pelvic organs in women, and of the prostate and seminal vesicles in men may demand operative treatment if the evidence of infection is clear cut. Many observers have reported patients with Graves' disease whose symptoms were relieved following the removal of genital tract infections. Common sense with avoidance of extremes should be the guide in handling the problem of focal infection.

Drug Treatment.—There is at present no specific remedy for Graves' disease. Almost every drug in the pharmacopeia has been employed in its treatment, but there are very few that have any established value. Quinin hydrobromate, the use of which was popularized by Forchheimer in this country, has been most constantly advocated. Forchheimer recommended the administration of 0.3 gm. of quinin hydrobromate and 0.06 gm. of ergotin in gelatin-coated pills four times a day. He claimed that the most striking result was a slowing of the pulse rate followed by a decrease in the tremor, exophthalmos, and in the size of the goiter. This result is difficult to explain from our knowledge of the pharmacology of quinin; nevertheless the empiric use of the drug is justified.

Sedatives may be indicated to allay nervous symptoms, and the bromids are the most useful for this purpose. They may be given in doses of from 1 to 2 gm. several times a day. At times they may profitably be combined with tincture of valerian. Opium or its derivatives should never be administered because of the danger of producing narcotic addiction. In patients in whom the disease appears to have a syphilitic origin, anti-

[1] The experimental researches of Reid Hunt indicate that organs, such as liver, should be entirely abstained from and that oatmeal has a stimulating effect on the thyroid.—Editor.

syphilitic treatment should be employed. The indications for this may be very clear in some instances, but in others, particularly when congenital lues is responsible for the disorder, it may require careful clinical judgment to suspect the specific origin of the disease. All doubtful cases should be given the benefit of a thorough course of mercury and arsphenamin. These remedies are occasionally followed by a remarkable recession of symptoms.

Opotherapy.—Many different kinds of opotherapy have been recommended but few have proved of value. The administration of thymus, recommended by Mikulicz in 1895, is of doubtful utility. The milk and serum of thyroidectomized animals and the so-called cytotoxic serum are worthless. The use of desiccated ovary and corpus luteum has given good results in certain cases. Desiccated suprarenal gland was first used by Solis-Cohen. Recently, Shapiro and Marine have reported very rapid and striking improvement in the general nutrition in a case of exophthalmic goiter following the use of fresh (ox) suprarenal cortex. They recommend the administration of 5-gm. doses of the fresh cortex daily by mouth. Larger doses, especially the whole gland, caused nausea and vomiting, probably from direct irritation of the gastric mucosa by epinephrin. A larger series of unpublished cases has given similar results. The chief gain is in the general nutrition, the improvement of muscular strength, and the control of diarrhea. There has been little immediate effect on the basal metabolic rate or on the pulse rate. Glycerol emulsion of the fresh suprarenal cortex has given equally good results. This preparation is of most value in the exhaustive stages of Graves' disease.

In certain cases of exophthalmic goiter which are beginning to manifest some of the signs of myxedema, the administration of very small doses of iodin or of thyroid extract is of value. Syrup of hydriodic acid, given in 5 drop doses daily, or a total of 0.5 gm. of desiccated thyroid given in 0.05 gm. doses daily should be given. During the administration even of these doses, the patient should be observed closely for any exaggeration of the symptoms of Graves' disease.

In 1911 Marine and Lenhart reported a series of cases from Crile's clinic showing that the administration of small doses of iodin (5 drops of syrup of hydriodic acid) for some weeks or months before operation made the operation easier by reason of the thyroid involution induced, greatly reduced the postoperative temperature and pulse reaction (the so-called postoperative hyperthyroidism of earlier writers), and, in the series reported, caused a significant reduction in the operative mortality.

Recently Plummer and Boothby (1924) have reported a series of 600 cases in which much larger doses of iodin (10 drops of Lugol's solution daily) were used for two or three weeks prior to operation. They report a definite reduction in the metabolic rate, the pulse rate, and a striking decrease in postoperative reaction in the majority of cases. None of the

cases was made worse. They prefer Lugol's solution to all other preparations of iodin for this phase of the medical treatment prior to operation.

Acidosis.—Acidosis is an occasional serious complication of Graves' disease. It occurs most frequently after operation but may appear after Roentgen treatment of the gland, during intercurrent infections, associated with severe vomiting and occasionally with diabetes. The condition is recognized clinically by an intense thirst, acetone odor to the breath, presence of acetone and diacetic acid in the urine, and a diminished carbon dioxid combining power of the blood-plasma. It should be combated by the administration of large amounts of water, sodium bicarbonate and glucose, which, because of the vomiting, must usually be given by proctoclysis; 500 c.c. of a solution containing 5 per cent each of sodium bicarbonate and glucose should be administered at intervals until the acidosis is under control. Thalhimer recommends insulin hypodermically in addition to the glucose.

Cardiovascular Symptoms.—It may be necessary to employ specific measures to control some of the symptoms referable to the heart. General treatment, including rest, is of the greatest importance. With an overactive heart an ice-bag to the precordia may be indicated. Digitalis or its derivatives are of no value in the control of tachycardia before irregularity of rhythm sets in. In the milder cases, when the patient is up and about, exercise must be limited sufficiently to prevent the appearance of dyspnea. When auricular fibrillation and myocardial insufficiency appear, the treatment corresponds to that of ordinary heart disease. It is at this stage that digitalis proves of value. With auricular fibrillation sufficient digitalis should be administered to control the pulse deficit and to reduce the pulse rate to as close to 72 as possible. The auricular fibrillation of exophthalmic goiter lends itself particularly well to successful treatment with quinidin hydrochlorid. A preliminary dose of 0.2 gm. is given to determine whether or not the patient has any idiosyncrasy to the drug. If there are no unfavorable symptoms, treatment may be commenced the following day, 0.4 gm. of the drug being administered every two hours until the pulse becomes regular and normal sinus rhythm is established, or until signs of intoxication become manifest. One must be particularly on the guard for sudden tachycardia, which may indicate the imminence of ventricular fibrillation. Other signs of intoxication are nausea, headache, vertigo, mental depression or excitement, and very rarely slowing of the respiration.

Gastro-intestinal Symptoms.—Severe vomiting must be controlled by absolute rest and the administration of the glucose and sodium bicarbonate by protoclysis, described above. In some instances gastric lavage is of value. The diarrhea frequently resists all local treatment and is relieved only when the general Graves' syndrome is under control. In patients suffering from diarrhea the diet must be bland. If the gastric analysis

indicates the presence of anacidity, hydrochloric acid in doses of about 0.5 c.c., well diluted, should be administered after meals. Fresh suprarenal cortex emulsion and even desiccated whole suprarenal gland is useful in controlling the diarrhea.

Roentgen Treatment.—Roentgen radiation of the thyroid gland is of little value in the treatment of Graves' disease. In this country Means has devoted particular attention to this form of therapy. He has recently published a series of 44 cases of complete and 12 cases of incomplete Graves' disease, of which two-thirds showed either recovery or improvement coincident with the treatment. The remaining third did not improve nor did they grow worse. Improvement was measured by a fall in the pulse rate and the basal metabolic rate, and by a gain in weight. In a series of 15 cases treated from five to seven years ago 2 were improved, 7 were well, 3 had died, and 3 could not be traced.

Although cases have been reported by others, in which the symptoms were aggravated by treatment, in the severe cases the operative risk is still greater. Major has recently described severe acidosis following radiation of the thyroid gland in Graves' disease. One disadvantage of the Roentgen treatment is that periglandular adhesions may form, making subsequent operation more difficult. Temporary or permanent myxedema may follow excessive dosage.

For radiation the neck is divided into three areas, right, left, and middle or suprasternal. A dosage equivalent to two-thirds the erythema dose for a normal skin is employed. This is just under the erythema dose for patients with Graves' disease who are more susceptible to the rays than normal individuals. The exposure is repeated once every three or four weeks, using a different neck area at each application.

Halsted, among others, has reported good results from Roentgen ray applications to the thymus, particularly in patients who were not cured by a double lobectomy. Roentgen ray treatment of Graves' disease is indicated when general medical measures are ineffectual and when the patient refuses operation. In severe cases in which the operative hazard is great, preliminary Roentgen ray treatment may be tried. Means claims that previous irradiation does not usually make the operation more difficult.

Surgical Treatment.—Operation is indicated when the conscientious employment of medical measures over a period of from one to two months has brought about no improvement and when the disease appears to be progressive in spite of attempts at its control. Such a criterion at once introduces a large personal equation, for the number of cases coming to the surgeon, if these indications are followed, will depend in large part on the skill of the physician who first sees the case. In patients whose economic condition prevents adequate and prolonged medical treatment, operation may be the only resource available. When operation has

been decided on, one should first endeavor, through the use of the measures outlined above, to improve the condition of the patient as much as possible. It is well to administer alkalis in the form of sodium bicarbonate on the day before the operation, in order to combat the possible acidosis. More important still is the choice of a surgeon. The operation of choice is subtotal thyroidectomy. In patients with a pulse rate constantly above 130 and with much emaciation a preliminary ligation of the thyroid arteries may be necessary. As an anesthetic, nitrous oxid and oxygen, combined with the use of novocain, appears to be the most satisfactory (Crile).

The postoperative treatment is most important. The immediate danger is the postoperative reaction, which is manifested by fever sometimes reaching 107° F., and acidosis. When such a reaction occurs it must be combated symptomatically. Morphin and atropin, an ice-bag to the heart and an alkaline Murphy drip, and glucose intravenously are the best measures at our command.

When a patient is convalescent from the operation he must continue under medical supervision for many months. The beneficial effects of a successful operation are manifested by a reduction in the pulse rate and basal metabolism beginning during the second week, as well as by the diminution of the other symptoms. Exophthalmos is rarely completely relieved. The best results and lowest mortality are obtained in the secondary cases with long-standing adenomatous goiters. Partial thyroidectomy is the only known means of rapidly reducing the metabolism. This effect of thyroidectomy is the same in a normal individual as in an exophthalmic goiter patient. The general tissue rest brought about by the reduced metabolism is valuable because it gives the patient a chance to regain regulatory control of the various organ activities. Most cases improve temporarily but unless the physiological rest is sufficiently prolonged to restore the balance, recurrence, particularly in the primary form, is probable and this is the most serious drawback to operations.

Results of Treatment.—The results of any particular plan of treatment of Graves' disease are very difficult to evaluate. The published statistics are of little value because of the varied types of cases included in the same series and because of various interpretations of the word "cure." Thus Forchheimer claimed that he treated 76 cases by medical means only, with no deaths and good results in from 70 to 90 per cent. Baker described 50 cases treated by medical measures, of whom 44 were alive on the average of 8.7 years after they were first seen. Of the 6 who died, none died of Graves' disease itself. The surgeons with great experience report an operative mortality of from 2 to 3 per cent. Kocher, in a series of 1,100 cases, states that 45 per cent were cured permanently and absolutely, 41 per cent were so improved that they could again work but were not completely cured, and in 11 per cent the result was poor.

CHAPTER XII

DISEASES OF THE PARATHYROID GLANDS

WILLIAM N. BERKELEY

Outline of Anatomy and Physiology.—A brief review of the anatomy and physiology of the parathyroids is almost essential to an understanding of disease in these organs and its treatment. In man the glands are usually four in number; exceptionally two, three and five are found, and I once noted six. Each gland is about as large as a grain of maize (6 by 4 by 2 mm.). It is generally flattened like a melon seed but may be ovoid or spherical. It is softer than a lymph-node of the same size, reddish-yellow or brownish-yellow in color, and has a thin fibrous capsule with characteristic venous tracery. Four glands will ordinarily weigh 35 to 40 mg.; sometimes, when very fatty, considerably more. They usually lie two on each side of the neck, embedded in fat, one above, and one below the middle of the posterior border of the thyroid lobe of the same side. They are rather close to the end twigs of the inferior thyroid artery, and are apt to fit into notches on the rear edge of the larger gland. The upper left gland is often deeper than its fellows, lying against the spine at the depth of the posterior border of the gullet. One or more glands are said to be sometimes found 2 inches lower than the thyroid in the neck, and sometimes on the contrary even embedded in the thyroid substance. In 130 autopsies on human subjects in which the parathyroids were removed, such positions were never observed by the writer.[1]

Histology.—The fine structure of the parathyroids is much like that of the pituitary and of the adrenal cortex. The secreting cells are grouped in solid anastomosing columns supported by loose and often fatty con-

[1] When removing the glands at autopsy one should follow Petersen's suggestion: cut away *in toto*, through the inlet in the thorax, the windpipe, gullet, thyroid, larynx and tongue, working carefully up against the cervical spine so as to remove the entire contents of the front of the neck between the skin and the backbone. Laying the mass thus obtained on a board—gullet up and thyroid down—the tissues above, below, and behind each thyroid lobe are thoroughly traversed with forceps and scalpel. Everything is put by that looks suspicious, the microscope being appealed to in doubtful cases. Bits of fat and thymus, small lymph-nodes, and small accessory thyroids confuse the beginner. Experience largely overcomes these difficulties.

nective tissue. A complete recent account is given by H. Bergstrand. Rarely in parts of a section the cells lie in a circle around a minute lumen. The lumen does not contain blood but a homogeneous eosin-staining stuff thought to be gland secretion.

Morbid Appearances.—Fatty infiltration, sometimes extreme, moderate sclerosis, small cysts, hyperemias, hyperplasias (or adenomata) have been described. No large cellular tumors of the parathyroids have been definitely identified (Bergstrand). Pathological changes in the glands are mostly chemical and circulatory, and are not readily recognized with the microscope. Seemingly normal parathyroids present wide variations in appearance. No one who has examined the glands in less than fifty autopsies should trust himself to make a diagnosis of any pathological condition.

Function.—Surgical removal of one, two, or three parathyroids from a rabbit or dog, or other available animal, is followed by no signs except hypertrophy of the remaining gland or glands. Later removal of the remaining parathyroid tissue, or removal of all the tissue at one time is followed in from ten to thirty-six hours by salivation, tachycardia, enormously hurried breathing, tremors and rigidity of the voluntary muscles, convulsions, complete anorexia, albuminuria, and rapid emaciation. Death occurs in from one to ten days. Postmortem appearances are negative; death appears to be of toxic origin.

The syndrome is called "tetania parathyreopriva," or more conveniently parathyroid tetany. For the immense literature see Jeandelise, Pool, Erdheim, Beebe and Berkeley, Ochsner and Thompson, Bergstrand, and Boothby.

In my experience young rabbits have sickened much more severely than older ones when the parathyroids were removed. V. Horsley made the same note long ago of young dogs after "thyroidectomy." Horsley's "thyroidectomy" we now know to have been essentially a parathyroidectomy, for the large lobes of the dog's thyroid carry the parathyroids in close contact, and the many small accessory thyroids in the dog make the removal of the large lobes an entirely negative performance so far as resulting signs of athyroidism go. Sometimes an animal desperately ill for half a day slowly recovers, and develops no further symptoms. In such cases a remnant of gland accidentally left behind seems to have had time to hypertrophy.

Chemical Physiology.—The chemical physiology of the parathyroid glands is unsettled. W. G. MacCallum showed that a suitable intravenous dose of a soluble calcium salt relieves the spasms. He therefore concluded that the gland controls the calcium metabolism of the body. S. P. Beebe and the writer successfully repeated the experiment, but from a series of additional observations concluded that the calcium has only a "drug effect," and that the parathyroid glands very probably furnish

enzymes of prime importance in the intermediary metabolism of nitrogen. This opinion has been strongly confirmed by Paton, Findlay and others. These observers found abnormally large amounts of a toxic congener of creatin, *guanidin,* or *methyl-guanidin,* in the urine and blood of animal subjects; by injecting these substances into normal controls they were able to produce a series of symptoms closely resembling parathyroid tetany. Hammett has set forth the most recent view of the subject.

CLINICAL FORMS OF PARATHYROID DISEASE

In medical literature for the past twenty years the parathyroids have been peculiarly the victims, so to speak, of unscientific observation. The "office desk scientist," the careless and superficial reviewer of literature, the laboratory man who never studied that chapter in logic which treats of fallacies, have done great harm. A mixed multitude of metabolic and convulsive disorders have been laid at the door of the parathyroids, and been "successfully treated" by a miscellaneous assortment of untested and unstandardized commercial and "home-made" preparations of the same gland.

To the busy practicing physician for whom this volume is written I make no apology for omitting mention entirely of all these products of loose thinking. There are no known clinical types of *hyperparathyroidism,* and as connected with *diseased or deficient parathyroid secretion,* only two diseases deserve mention at the present time, *tetany,* and *paralysis agitans.*

Tetany

Postoperative Tetany.—This is a dangerous condition, fortunately rare, developing after operation upon the thyroid gland, in the course of which the parathyroids have been also removed or have been seriously injured. The condition has received much attention of late years from surgeons (Kocher, Halsted, and a host of others).

Symptoms.—Symptoms, when beginning early and acutely, are similar in many ways to the parathyroid tetany of animals, though, of course, not all the signs will be presented by a single patient. Dreadful restlessness, mental distress, delirium, and insomnia are superadded. Signs of idiopathic tetany can at times be observed or elicited (see page 147). Occasionally early and severe symptoms gradually subside. The reason probably lies in the fortunate restoration to function of some damaged fragment of gland left behind. Many cases go on to a fatal termination. Death is sometimes sudden.

A remarkable *late case* is reported by A. F. Hurst. The patient was a clerk, forty-seven years old, when first seen. At thirty years he noticed

a gradually growing thyroid struma. This was later excised. He was well for two years after the operation and weighed 191 pounds. He then rather suddenly became depressed, nervous, tremulous, restless, and could not sleep. There was fibrillary twitching of the eyelids but no tetany. His pulse was 120. He had an abnormally large appetite but rapidly fell away to 141 pounds and less; there were three or four stools a day. He became impotent. His hair stopped growing and grew thinner. He was much tormented by dysphagia and colic. He recovered with almost miraculous speed on parathyroid medication. Relapses occurred once or twice after omission of the medicine, but he was well at last reports and had discontinued the parathyroid treatment for a good while.

Treatment of Postoperative Tetany.—Prevention cannot be too much emphasized. Thyroid tumors should be excised only by surgeons who are fully advised of the regular and the *anomalous* situations (see page 143) of the parathyroid glands. Should the accident be observed during operation, the gland should be at once aseptically replanted, not in the operation wound, but in some other well-vascularized part of the patient's body. Such grafts (isotransplants) are the only ones which give chance of permanent and successful growth. To be perfectly sure of the facts a bit of the supposed parathyroid should be retained for microscopic examination.

When postoperative symptoms give evidence that the accident has occurred, a physiologically tested parathyroid preparation should be given hypodermically and *per os* in the hope of tiding the patient over the critical period necessary for hypertrophy of some fragment of parathyroid that may by good luck have survived destruction.

Grafting a gland from a suitable human donor may be considered, but very few successful cases of such grafting have been reported, so few that doubt may well be cast upon all. In some cases the grafts were not even microscopically identified. It has not been proved that the grafting of a gland, even from one member to another of the same family, is possible, much less from one man to another who is unrelated. Successful transplantation of animal glands into a human being is believed to be entirely impossible by scientific workers best qualified to express an opinion. The human donor himself, if such can occasionally be found, runs a serious chance of irreparable harm; and the difficulties of identifying a parathyroid gland at the bottom of a deep, bloody and pulsating hole in the neck are practically insuperable except as an occasional fortunate accident.

Glands removed at an early autopsy have also been used. Brown reports a typical experience. Three autopsy glands were planted in the patient's sternomastoid muscle. She was greatly improved for several months, then rather suddenly relapsed, and died. Microscopic examination of the grafts showed that they had become largely fibrous, and "were probably not functioning."

Besides gland therapy, and gland grafting, an attempt should be made to relieve the patient's symptoms by *sedative drugs*. Soluble calcium salts may be given intravenously (see page 148). Death being sometimes sudden, the patient's friends should be warned of the gravity of his condition.

Idiopathic Tetany

(*Endemic Tetany, Epidemic Tetany*)

Causation.—The causal nexus between idiopathic tetany and the parathyroids is not scientifically established. Swale Vincent still doubts it. Jeandelise first suggested it in 1902. Pineles, Erdheim, and W. G. MacCallum followed up the subject, none of them successfully explaining all the facts. But the parathyroid hypothesis may be accepted as the most probable yet offered. Predisposing causes are dilatation of the stomach, pregnancy, and, in children, rickets, intestinal disorders, and worms.

Distribution.—In America hardly 100 adult cases have been reported; in small children it is more common. On the continent of Europe it occurs frequently at all ages. Friedrich Kraus used to show many cases in Vienna in former years, and he remarked upon the curious frequency with which it attacked young shoemakers' apprentices, sometimes almost in epidemic form. McCarrison describes it as an endemic disease in the Himalayas, especially among childbearing women, and almost exclusively in the spring months. Special clinical types are described as incident upon gastric dilatation, upon pregnancy, and in children upon rickets. Von Hochwart connects it also with acute infectious diseases, and with certain cases of chronic poisoning.

Symptoms and Diagnosis.—The disease is marked essentially by increase in the excitability of all the nerves, sympathetic, sensory and motor; but the motor signs (spasms) are those most easily observed. Spasms are tonic, with intermissions; they are local or general, often bilateral. A sharp tap on the trunk of the facial nerve in front of the ear produces a variably strong contraction of the facial muscles on the same side (Chvostek's sign). Prolonged compression of the trunk of the brachial nerve in the arm (three to five minutes is advised by Hochwart and again emphasized in L. F. Barker's recent exhaustive study) often produces the *main d'accoucheur* or "obstetric hand." The fingers are extended and clumped, the thumb in the palm (Trousseau's sign). In severe cases a blow on a nerve trunk precipitates a general tonic convulsion which may last for hours. The patient remains conscious and suffers great pain. Usually there is no continuous tremor. In infants and small children the symptoms may be confined to bilateral carpopedal spasms (*arthrogryposis*). These may be quite persistent, and the child screams with the pain. Laryngismus is present at times. General convulsions may

also occur, and a fatal result is not unknown; but the cases in infants are usually benign, the symptoms disappearing in a few weeks when treatment is instituted.

The diagnosis must be based upon an intelligent interpretation of the signs. Carpopedal spasm simulating tetany appears from time to time temporarily in a wide diversity of diseases which have no relation to tetany or to one another. Tetanus may be distinguished by the early appearance of *trismus,* which is not often seen in simple tetany. Hysterical contractures will probably coincide with signs of hysteria elsewhere.

Treatment—*In adults.*—During the existence of active symptoms the administration of parathyroid gland, properly prepared and standardized (see page 151), often gives good satisfaction. In urgent cases where the stomach is dilated or the bowels disordered, oral administration is of doubtful efficiency, and the hypodermic injection of gland extract is more rational. In recent years two severe cases in adults in care of James (Roosevelt Hospital, New York) and Kinnicutt (Presbyterian Hospital, New York) did well on parathyroid preparations supplied by S. P. Beebe and the writer. Intravenous injections of 1 or 2 gm. of calcium lactate in solution (Moffitt recommends much larger doses) relieve the spasms temporarily. Commercial preparations of calcium lactate seem to vary in solubility, and therefore the solubility of the preparation to be used should be determined beforehand. An aqueous solution of measured strength is filtered clear, then boiled in a sterile plugged test-tube for ten minutes, cooled to 100° F., and carefully and slowly injected *secundum artem* into a convenient vein. The technic must be correct; calcium lactate in the tissues makes a severe and painful induration, sometimes an abscess. Calcium salts by the mouth are so imperfectly absorbed that oral administration is of doubtful value. The patient should be put to bed, protected from worry, and carefully nourished on a diet suitable to the individual case. As parathyroid tetany is equally severe in cabbage-fed rabbits and meat-fed dogs, it is difficult to say that meats ought always to be excluded from the diet. Circumstances must decide this question.

In pregnancy the condition is not usually sufficiently serious to require abortion; certainly milder methods should be tried first. Besides the remedies already mentioned warm baths, suitable amounts of bromids, ¼ to ⅛ gr. of luminal *per diem* and careful attention to the bowels may suffice. In dilatation of the stomach lavage may be cautiously tried. It is said that gastric tetany is sometimes aggravated by lavage. For the proper surgical methods in this disease the surgical textbooks must be consulted.

In Children.—The infantile form of the disease appears most frequently before the second year. Parathyroid preparation may be given, but the obvious association of the condition with rickets and intestinal

disorders gives a practical "lead" to the treatment which should be promptly noted. Revision of the milk formula, correction of the bowel disorder, and the giving of cod-liver oil are the first measures to be instituted. Some cases have recovered promptly after the administration of a vermifuge. Laryngismus, as a symptom of tetany, is to be treated as elsewhere. Warm baths, small repeated doses of the wine of ipecac, proper doses of bromids, and inhalations of hot-water vapor from a croup kettle should be promptly prescribed. General convulsions may be treated with warm bathing, and in severe cases chloroform inhalations should not be delayed. Fortunately convulsions are not often so suddenly fatal as to forestall treatment.

Paralysis Agitans

(*Parkinson's Disease, Shaking Palsy*)

Symptomatology.—It is over one hundred years since James Parkinson's classic account of shaking palsy was first published. The author, in his preface, remarks with truth and feeling:

"The disease respecting which the present inquiry is made is of a nature highly afflictive. . . . The writer will repine at no censure which the precipitate publication of mere conjectural suggestions may incur, but shall think himself fully rewarded by having attracted the attention of those who may point out the most appropriate means of relieving a tedious and most distressing malady."

The malady is still tedious and most distressing. The essential symptomatic feature is *increased muscular tone.* When the muscle-contracting impulses are *clonic,* the feature of the disease from which it has derived its common name of "shaking palsy" is manifested. When the impulses are *tonic,* there is a pronounced and permanent muscular rigidity, *paralysis agitans sine agitatione.* The latter is a graver form of the disease. The two types may coexist. In 95 per cent of the cases the tremor is absent in sleep. The tremor is slow (3 to 6 vibrations per second), aggravated by excitement, and controlled only momentarily by mental effort. The trouble begins, as a rule, in one extremity, in the thumb, or forefinger, or great toe, and spreads thence in the lapse of weeks and months to adjacent groups of muscles in the same limb, and to other parts of the body. The arm and leg of one side may be simultaneously affected, producing a "hemiplegic form" of the disease which often deceives the inexperienced observer. The slow onset, unaltered tendon reflexes, and characteristic tremor are ample differential signs. Speech is labored; the face is masklike (Parkinson's mask).

Propulsion and retropulsion are familiar. Muscular and fascial pains

are often tormenting. Restlessness is a common symptom. Drooling is not infrequent. Hot and cold "flashes," or a persistent local or general sense of heat or cold may add to the patient's misery. The mind remains unaffected.

Etiology.—Sex is immaterial and no race is exempt. As to age, cases under forty years are rare, and under thirty very rare. The few cases reported around twenty (H. Willige) have probably an exceptional causation. Lues is not associated with the disease in 10 per cent of the cases. Autopsies have been vague. Camp believed he had found a primary lesion in the muscles; Hunt has reported a case of the "paralysis agitans syndrome" beginning at fifteen years. The autopsy showed "destructive lesions of several groups of cells in the globus pallidus." This observation has been partially confirmed recently by French writers, but further investigations must show whether this concurrence of symptoms and lesion is common, and whether the relation of one to the other is causal. Hunt also believes that the young patients constitute a special type, and that further study may differentiate many of the older cases.

The widely distributed outbreak of epidemic encephalitis in 1918 has complicated the question still further. In this disease a "paralysis agitans syndrome" occasionally appears which is entirely different etiologically from the ordinary clinical form. For the treatment of the encephalitis cases nothing is now known.

The confusions and contradictions of autopsy reports long ago led Dana and others to advance the view that a chronic toxemia is the cause of the disease; and it was suggested by Lundborg of Stockholm in 1904, and by the writer independently in 1905 that a *chronic dyscrasia or insufficiency of the parathyroid glands* lies at the base of the disease. The reasons for this view may be summarized as follows:

1. The symptoms appearing in rabbits and other available experimental animals upon removal of the glands are suggestive. Vetlesen discusses the matter at length and concludes:

"It is experimentally proved (especially by Tanberg) that by operation on animals a special chronic form of parathyroid insufficiency may be produced which clinically presents a striking similarity to paralysis agitans in man."

2. The disease has been reported many times in myxedema, and sometimes in exophthalmic goiter, where the contiguity of the diseased thyroid may well be supposed to work mischief to the parathyroids, or interfere with their blood supply.

3. The parathyroids have been reported in a diseased condition in a fair proportion of the autopsies on the disease.

4. A properly prepared extract of parathyroid has been found of remarkable benefit in a good majority of the cases treated.

While these considerations do not amount to a demonstration, the hypothesis certainly comes within the bounds of reasonable scientific speculation.

The parathyroid theory has been received with considerable favor by the profession. In the International Clinics for 1912 I reviewed the literature, mostly favorable, to that date. Since then Greenwald has advanced some inconclusive chemical observations *against* the parathyroid theory. Troemner thinks the parathyroid hypothesis "possible"; and Schioetz defends it with considerable warmth.

Diagnosis.—The diagnosis of the disease is not very difficult. It is to be based upon a reasonable concurrence of the signs above noted. Hemiplegia gives increased reflexes on the paralyzed side. *Tremor senilis* is unaccompanied by rigidity, pain, or any other of the symptoms of shaking palsy. Early cases with tremor of intention as the only sign (Gowers) are more perplexing, but time will soon tell.

Treatment with Parathyroid Gland.—An efficient preparation can only be made from perfectly fresh and accurately identified glands. Bullock glands are practically the only ones available in America. That the animal used is a castrate is objectionable on endocrinological grounds, but the resulting extract seems nevertheless efficient. Fresh glands by the mouth are sometimes successful, but they are of doubtful digestibility and full of fat and of course are rarely available.

Extracts for clinical use should be standardized. This requirement may be roughly satisfied by noting the minimum amount of the extract which when injected hypodermically in a rabbit or dog of known weight will relieve the symptoms following parathyroidectomy for a given time. The test must be made twice to exclude the synergic effect of growing remnants of gland possibly left behind at operation. Commercial extracts are often "defatted" with acetone. This removes the fat, to be sure, but it also removes much of the active principle. Many commercial extracts may be given by the teaspoonful without effect. They are made mostly of thymus, thyroid and lymphnodes.

Chemical details of my own extraction process have been repeatedly published and need not be again detailed here. The formula is manufactured by several New York wholesalers. It comes in small tablets (1/50 gr. of extract in milk or cane sugar), and as a hypodermic solution. The latter is marketed in small rubber-stoppered phials of five mils. The hypodermic solution is the ideal preparation, but is more expensive, and many patients do very well on the tablets. The dose by the mouth is one tablet two to six times a day, preferably after eating. The hypodermic solution is given in doses of 1 to 2 mils once or twice a day. One mil contains 1/50 gr. of the extract. This mixes metric and English systems but is justified by its convenience, and is easily remembered. The solvent is physiological salt solution. A trace of chloroform is added as a pre-

servative. Aseptically injected the hypodermic solution should be absolutely without local reaction.

The *benefits of treatment* usually appear slowly. They consist in lessened rigidity, relief or arrest of the shaking, restlessness and insomnia, and the abolishing of salivation. In some of the cases now and then quite a miracle is performed, for example, in a recent case reported by Martyn. The patient, whose condition had been desperate, was so remarkably benefited that he was enabled to bathe and dress himself, read and write comfortably once more, sleep well, and amuse himself by pruning his own orchard trees again—a pleasure in which he had not been able to indulge himself for a long time. The only setback was for a week or so when he was unable to get a fresh supply of the medicine.

The writer recently reported two cases which attracted his special notice. One of them, father of a medical associate in New York, was literally kept alive by parathyroid for ten years.

A medical correspondent in Cleveland wrote of a notable transformation in the case of an elderly woman under his care, who received fresh glands daily. She rose from bed where she had lain for a long time like a wooden image, began again to dress and feed herself and walk about without assistance. She resumed her former erect posture, and even recovered her singing voice. Her improvement was only once interrupted when fresh glands were for a time replaced by a commercial powder.

Of another elderly patient living near New York his daughter wrote me, "I should dread to contemplate my father's declining years without the help the parathyroid has given him." The wife of another recent patient wrote, "He is greatly improved; we hope he will yet be entirely well."

Contra-indications are few or none. Cardiac and arterial disease may even be benefited. Personally, in many years and with more than 200 patients, I have seen only one who could not take parathyroid, that is, ox-parathyroid. He possibly had an anaphylactic sensitiveness to the foreign proteins. This may also have been the case with a patient in the care of Parcher, whose account (personal communication) mentioned somewhat similar symptoms.

Some patients become "nervous" and shake worse when the dose is pushed too rapidly. In such cases the remedy should be given in divided and infrequent doses until they have become accustomed to it. I have had one patient who was sure the parathyroid constipated him, but he overcame this very easily with a laxative.

Improvement is often noticed in two weeks, very generally in two months; it should continue for a few months more. After this one should still give the remedy, but in smaller doses—just enough to maintain the benefits already secured. There is never a "cure," any more than there is in cretinism treated with thyroid; but 60 to 70 per cent of the

patients who have received real parathyroid have done very well for years, and have found no very great inconvenience in the necessity of continuing the medication.

Failures of the Parathyroid Treatment.—Institutional cases rarely do well. The reasons need not be amplified. But after great good luck with four or five patients there usually come two or three more who are entirely unaffected either by the oral administration of the tablets or by two or three hypodermic injections a day. Some patients do well for a year or so, and then rapidly fail. Physicians who have seen only two or three failures are pessimistic. Those who have seen only two or three brilliant successes are just as unduly optimistic. The truth lies between, and the causes of failure are only conjectural. The explanation possibly lies in the chemical differences between human and animal parathyroids. Beebe called attention some years ago to the possibly analogous fact that *human thyroids* are much more efficient in *hypothyroid* conditions in man than are any animal preparations.

Other Remedies.—The successes and failures of *hyoscin* are an old story. The alkaloid is best given in very small doses as hyoscin hydrobromate. One two-hundredth of a grain is enough. It may be taken two or three times a week to help the patient over a hard place—a journey, a business interview, a dinner party, a church service. *Hyoscyamin* was preferred by Starr. Overdosing is dangerous; delirium, urinary retention with overflow, and the other signs of belladonna poisoning may result. Once in a long while *duboisin* is more efficacious than hyoscin.

The hypodermic use of *arsenic* has been recommended, the usual form of the drug being sodium cacodylate (1 to 5 gr. daily). It is occasionally helpful, but it is very uncertain. Bromids and antispasmodics are mostly futile. For the chronic and obstinate constipation, aggravated by the stiff pelvic muscles, some form of Rhamnus purshiana is usually to be preferred. The diet, of course, should be laxative. High enemata occasionally render good service. Intravenous injections of calcium lactate (see page 148 for technic) in two patients in whom the drug in various doses was faithfully tried out at my Clinic did no permanent good.

Remedial agencies other than drugs have a place in the treatment. *Warm baths,* temperature 100° F., at bedtime several times a week are helpful, promoting elimination and inducing comfortable sleep. If the patient likes sea salt in the bath, it should by all means be provided. General massage and passive motion of the stiff and helpless limbs should be persevered with. *Massage of the front of the neck, however, is by all means to be avoided.* By liberating thyroid into the system it makes the patient rapidly worse. This is probably why so many of my patients, as they tell me on the first visit, have been "almost killed" by the osteopaths. Easy travel is helpful, and active exercise, walking, horseback-riding, motoring, is to be advised when the disease is not too far advanced. The

patients are appreciably sustained by cheerful company and a hopeful environment. They should by all means be kept out of a hospital atmosphere.

There are no special dietetic indications other than those applicable to old age in general, or complicating diseases. I have never been able to see that any special dietetic regimen was of benefit. I have tried a full meat diet (100 gm. of protein per day), an exclusive vegetable diet, a diet rich in calcium, a diet poor in calcium, but without any observable effect. If the patient has been used to the moderate enjoyment of alcoholic beverages all his life, there is no objection to the temperate continuance of them.

As the gravest cases may unexpectedly at times have spontaneous periods of remission, the medical attendant is justified in striving at all times to maintain an attitude of hopefulness in the sick-room.

REFERENCES

Barker, L. F. Endocrinology and Metabolism, D. Appleton & Co., New York, ii, 1922.
Beebe, S. P., and Berkeley, W. N. Journ. Med. Res., 1909.
Berkeley, W. N. N. Y. Med. Journ., 1905.
——— Presbyterian Hosp. Rep., New York, 1906.
——— International Clinics, 1912.
Bergstrand, H. Acta Med. Scandinavica, lii, 1919-1920.
Boothby, W. M. Endocrinology, July, 1921.
Brown, A. E. Ann. Surg., lxxv, 1922.
Camp, C. D. Journ. Am. Med. Ass., April 13, 1907.
Erdheim, J. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xvi, 1906.
Gowers, W. R. Diseases of Nervous System, London, 1893.
Greenwald, J. Am. Journ. Med. Sc., 1914.
Halsted, W. S. Johns Hopkins Hosp. Rep., xix, and elsewhere.
Hammett, F. S. N. Y. Med. Journ., 1922.
Hochwart, L. Frank von. Die Tetanie, 2d ed., Wien and Leipzig, 1907.
Hunt, J. R. Proc. Am. Neurol. Soc., Washington, 1916.
Hurst, A. F. N. Y. Med. Journ., cxv, 1922.
——— Guy's Hosp. Rep., 1913. Practitioner, xciv, 1915.
Jeandelise, P. Thèse de Nancy, 1903.
Kocher, T. Arch. f. klin. Chir., xcii, 1910, and elsewhere.
Lundborg. Deutsche Ztschr. f. Nervenh., 1904.
MacCallum, W. G. Centralb. f. allg. Path. u. path. Anat., May, 1905.
——— Johns Hopkins Hosp. Rep., 1908.
McCarrison, R. The Thyroid Gland, London, 1917.
Martyn, George. The Link, Los Angeles, Feb., 1917.

Moffitt, H. C. Journ. Am. Med. Ass., lvii, 452, 1911.
Ochsner and Thompson. Treatise on Surgery and Pathology of Thyroid and Parathyroid Glands, St. Louis, 1910.
Paton, D. N., Findlay, Watson, Burns, and Sharpe. Quart. Journ. Exper. Physiol., x, 1916-1917.
Petersen, Hugo. Virchow's Arch., clxxiv, 3, 1903.
Pineles, F. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xiv, 120, 1904-1905.
Pool, E. H. Ann. Surg., 1907.
Schioetz. Ztschr. f. d. ges. Neurol. u. Psychiat., xxiii, 1914.
Troemner. Deutsche Ztschr. f. Nervenheilk., v, 53, 1914.
Vetlesen, H. J. Ztschr. f. d. ges. Neurol. u. Psychiat., xxvi, 1914.
Vincent, Swale. Internal Secretions and Ductless Glands, 2d ed., Longmans Green and Co., New York, 1922.
Willige, H. Ztschr. f. d. ges. Neurol. u. Psychiat., iv, 4, 1911

CHAPTER XIII

DISEASES OF THE THYMUS GLAND

KENNETH D. BLACKFAN

Introduction.—Pathological processes arising in a structure whose functions are so little understand as are those of the thymus gland necessitate a careful consideration of the nature of the disturbances which arise, of their clinical course and of the main points in their diagnosis, in order that principles recommended for the relief of the symptoms and for the restoration to health of the sufferer may be instituted. In this discussion the endeavor has been made to correlate the pathological processes which are attributed to disturbances of the thymus gland with the known facts regarding its development, functions and physiological processes, and to outline the therapeutic measures which have been established on clinical as well as experimental bases.

Origin.—The thymus in man originates in an epithelial growth from the diverticulum of the third pharyngeal pouch. With the appearance of this anlage, called Thymus III, the epithelium of the dorsal diverticulum proliferates and undergoes histologic differentiation into Parathyroid III. The mesial portion atrophies and disappears, so that Thymus III and Parathyroid III become independent structures. The thymus anlage or thymus cord elongates into a caudal and cranial end. The thin cranial end atrophies and disappears with the exception of the lowermost part, which persists and forms the cervical process. The caudal end becomes thicker, and, extending into the thorax, joins with the opposite side to form the thoracic thymus. The completely developed gland consists of the cervical and thoracic portions of the paired anlage.

Developmental Defects.—Failure of the thymus to follow, during fetal life, the developmental manner described above, either by arrest or cessation of growth, results in abnormalities which may have pathologic significance. Enlargements of the cervical process resulting from a failure of the cranial end to atrophy at the proper time; thymic rests becoming separated from the cranial end, but continuing to grow; and accessory nodules developing from the fourth pharyngeal pouch, are the more common abnormalities which have been described. When present, accessory nodules are situated in the neighborhood of the thyroid and parathyroid glands.

Structure.—The thymus is usually composed of two lobes, although conglomerate, trilobed and unilobed forms are not infrequently seen. The gland consists of a fibrous capsule, connective tissue trabeculæ, and a cortical and a medullary portion. During the developmental stage, the epithelial elements are invaded by ingrowing lymphoid tissue and blood-vessels and broken up into irregular islands. The latter become smaller and smaller, until finally the lymphoid elements predominate. The Hassall bodies represent derivatives from the primary epithelial elements. The true nature of these lymphoid and epithelial elements has not been determined. The lymphocytes are continually undergoing degeneration, and they and their fragments are constantly being taken up by the larger epithelial cells.

Involution.—Modification of the structure of the thymus during different phases of its growth is spoken of as physiological involution. From birth and often as late as the time of puberty it increases in weight and during this period the lymphoid cells are so massed together, that the cortex and the medulla are differentiated with difficulty. From puberty to adolescence there is a gradual lessening in weight, which continues throughout life. The differentiation between cortex and medulla can be made more readily during this period, owing to the reduction in the lymphoid elements and the prominence of the interstitial tissue and of the Hassall bodies. Gradually interstitial tissue and fat form the larger part of the organ. Adipose tissue containing remains of thymic parenchyma may be demonstrated even in individuals past the third decade of life.

Weight.—The weight of the thymus depends on a number of different factors. When determining by weight alone whether a thymus is abnormally enlarged, the age of the patient, the amount of adipose and connective tissue, and the relation of the thymus in weight to the other organs should be taken into consideration. The table of weights illustrates the changes which take place during different periods of life.

Weight of Thymus at Different Ages (Hammar)

Years	*Grams*
Newborn	13.6
1 to 5	23.0
6 to 10	26.1
11 to 15	37.52
21 to 25	24.73
26 to 35	20.0
35 to 45	16.0
56 to 65	16.8
66 to 75	6.0

Situation and Form.—The position and form of the thymus are altered during fetal life and infancy by change in growth, by the establishment of respiration and, during early adult life, by the processes of involution. During fetal life and persisting throughout infancy, the cervicothoracic thymus is the predominating type, the larger part lying within the thorax, and the smaller part extending upward to within the region of the thyroid. In adults the cervical portion is either very small or entirely absent. The thymus in late fetal life and in stillborn children is broad and its lateral surfaces are convex and bulge against the medial surfaces of the lungs. The lungs rarely extend on its anterior surface and the thymus seldom overlies the anterior surface of the right border of the heart. After the establishment of respiration, the thymus is molded, becoming narrowed and elongated by the expansion of the lungs, so that its anterior, lateral and posterior surfaces bear the imprint of all the organs with which it comes in contact. It usually extends over the right ventricle. The right auricle, veins, trachea, and esophagus are situated posteriorly. In infants and young children the anteroposterior diameter of the superior thoracic aperture is often not more than 2 cm. This has been referred to as the critical space of Grawitz. It is obvious that the structures situated posteriorly and the structures passing through this space might be compressed to such a degree as to interfere with their normal function, when the thymus, as the result of hyperplasia, cannot protrude freely through this aperture. Usually the two upper poles rise to within one-half inch of the thyroid. When the thymus is enlarged, it may reach the thyroid and in rare cases it extends as high as the hyoid bone. The main blood supply is derived from the internal mammary, innominate and intercostal vessels. The thymus is composed of a closed lymphatic system. The nerve supply is from the sympathetic system. The nerves terminate in the blood vessel walls.

Function.—From the time Vesalius suggested that the thymus gland served as a protecting pad to the intrathoracic organs, the function of the thymus has been the subject of much speculation. Many extensive investigations, both experimental and clinical, have been made to ascertain its purpose in the animal organism. Is it a blood-forming organ and does it produce lymphocytes? What is its relation to the body as an internal secretory organ? Is it essential to life? These and many other questions have been asked and answers given, as a search through a voluminous literature will reveal. As yet but few positive statements can be made regarding the function of this body.

Lymphocytic Function.—Although from a histologic aspect the thymus gland is a lympho-epithelial structure, this fact by itself does not disprove the theory that it functions in infancy and childhood as a lymphoid organ. While not functioning as a true hematopoietic organ, it is in all probability capable of producing lymphocytes.

Internal Secretion.—One might judge from the references in the literature to the internal secretion of the thymus and its effect on the various pathologic conditions of the body that a thymic hormone had been established without a doubt. Yet most of the experimental work to prove the existence of an internal secretion has given conflicting results. Various species of animals have been used experimentally for this purpose. It has been claimed that deprivation of the thymus in animals has resulted in death, with and without changes in growth and nutrition, and in alterations in the bony structure and in the glands of internal secretion. Other observers claim that extirpation of the thymus has resulted in transitory disturbance in growth and nutrition, while other workers have failed to find any pathologic changes in thymectomized animals. In a critical review, Park suggests that some of the causes for the conflicting experimental results are due to close confinement of animals, unsuitable food, failure to remove thymic rests, as well as improperly controlled experiments. He has drawn conclusions from most carefully controlled experiments which have a pertinent bearing on the effects of thymus deprivation. Park and his colleagues conclude that *the thymus gland is not essential to life in the dog. Extirpation of the thymus probably does not influence growth and development; neither does it produce alterations in the organs of internal secretion.* Inasmuch as these findings have been corroborated by many other workers, and convincing arguments have been advanced by which many of the positive results which have been reported can be explained, evidence gained by extirpation fails to support the theory of an internal secretory activity of the thymus gland. Similar results have been obtained by a large number of workers, who have used feeding experiments in animals. Certainly before admitting the existence of a thymic hormone, the subject needs to be investigated from a new point of view.

Relationship of Thymus to Diseases of Internal Secretion.—Much confusion regarding the pathogenesis of disease of the thymus likewise has arisen from conflicting statements pertaining to the function of this gland, based on animal experiments. The frequency with which an enlarged gland has been found in association with a number of pathologic conditions has been used as clinical proof of thymus gland disturbances. Clinicians have been altogether too eager to associate a disturbance of the thymus gland with exophthalmic goiter, myasthenia gravis, Addison's disease, polyglandular disturbances and status thymicolymphaticus. An enlargement of the thymus, due to alterations in the involutional process and to an unusual amount of adipose tissue, may be found clinically, or at necropsy, in these and other pathologic conditions. Their presence should not necessarily be taken to indicate an endocrine disturbance. Neither should atrophy of the thymus lead to the belief that there is a general metabolic disturbance, as it is well known that the thymus

atrophies rapidly in starvation and chronic diseases. Awaiting further proof of an internal secretion or a toxin elaborated by the thymus, the hyperplasia has to be regarded as due to failure of the thymus to undergo involution at the proper time, or to stimulation or renewal of growth, before or after involution has occurred. This hyperplasia, however, may actually constitute a complication which endangers the patient's life. Relief of the suffocative attacks by partial removal of the thymus, or by roentgenization or radiation usually is followed by prompt relief. Because of the frequency with which an enlarged thymus is associated with Graves' disease, partial removal of the thymus or postoperative treatment with Roentgen rays is recommended by many surgeons as a routine procedure following thyroidectomy.

Use of Thymus Preparations.—If, as the evidence points, the thymus gland has no internal secretory function, then the employment of preparations of the thymus gland in the treatment of those diseases in which there is an hyperplasia of the thymus has no rational basis. Clinical experience has demonstrated that the use of thymus extracts in various forms of thyroid disease, Addison's disease, myasthenia gravis, and many symptomatic conditions, has not been followed, as is to be expected, by gratifying results. Furthermore, no specific indications for the employment of extracts of the thymus in polyglandular preparations have been established up to the present time.

Status Thymicolymphaticus.—There is no convincing proof that the sudden death which so often follows trauma, anesthesia, fright or that the diminished resistance to infection are due to disturbances of thymic function. Preventive and curative therapeutic measures are purely speculative until the rôle played by hyperplasia of the thymus, in this condition is more definitely determined.

Hyperplasia in Childhood.—The frequency with which hyperplasia of the thymus unassociated with hyperplasia of other lymphoid structures has been found in infants and children dying suddenly, and as the underlying factor in the production of "thymic asthma" has renewed the efforts of investigators, and fruitful information has been obtained within recent years. It has been shown that an enlarged thymus is much more common in children than has been thought and that a diagnosis can be readily established by physical examination, confirmed by roentgenograms. By the use of Roentgen ray therapy, involution can be brought about with a disappearance of the symptoms in a large percentage of cases.

Symptoms.—The symptoms most commonly seen are cough, dyspnea, and laryngeal stridor. They may appear intermittently or occur continuously. If the dyspnea is not relieved, suffocative attacks with intense cyanosis, convulsions and death may ensue. In less severe attacks, the dyspnea, cyanosis and convulsive movements appear at intervals. Laryngeal stridor, which at first is inspiratory in character, usually becomes

expiratory if the dyspnea is not relieved. Frequently no symptoms are observed, the first intimation of an enlarged thymus being obtained at the necropsy of children who have been found dead.

Diagnosis.—The diagnosis of an hyperplasia of the thymus should be made in patients presenting any of the above symptoms when, by percussion, dulness is found to extend over seven-eighths of an inch to the left and over one-half inch to the right of the mid-sternal line in the second interspace. This dulness, as a rule, is continuous with the cardiac dulness below and it usually disappears with the head held in extreme flexion. Confirmatory evidence of an enlarged thymus is obtained when the roentgenogram shows a shadow to the right and left of the midsternal line, continuous with the heart shadow, either obliterating the normal cardiac angles or being superimposed on it as a broad cap. It must be borne in mind that enlarged bronchial glands, congenital heart disease, foreign bodies, tetany, congenital malformations of the larynx, et cetera, may be the cause of symptoms which are identical with those seen in thymic hyperplasia. Also a shadow is cast in the roentgenogram in a large number of otherwise *normal* children, which cannot be differentiated from the shadow cast in patients suffering from "thymic asthma."

Treatment.—A consideration of the treatment of hyperplasia of the thymus very naturally leads to a discussion of the manner of production of the symptoms. Having in mind the anatomical situation of the thymus and the narrow superior aperture of the thorax (the critical space of Grawitz) and that the thymus may exceed many times its normal weight, it is evident that disturbances of respiration and circulation from mechanical compression may be a determining factor in many cases at least. It has not been proved that the enlarged thymus interferes with the function of the nerves in this region, although this is a possibility which has to be taken into consideration.

Emergency Measures.—Drugs, thymus extracts and other remedial measures are not to be relied upon in the face of alarming and critical symptoms. Partial thymectomy or tracheotomy should be resorted to if the suffocative symptoms are threatening the life of the patient.

Specific Therapy.—Surgical procedures, however, should be resorted to less and less, as it has been established that the mechanical effects of the enlarged thymus can be altered by roentgenization. It has been shown, experimentally with animals and clinically in patients, that involution of the thymus can be brought about with varying degrees of rapidity from a very slight fibrosis to a complete sclerosis, depending on the number and frequency of exposures. When the question arises as to whether the symptoms are due to an enlarged thymus, or to other pathologic conditions, therapeutic treatment should be administered. Whether the Roentgen ray or radium is used, the involution of the thymus is the object to be attained.

Roentgen Ray Therapy.—Roentgen ray treatment may be given on successive days or at longer intervals, according to the degree of mechanical obstruction, as determined by the severity of the symptoms. Improvement of symptoms has been noted after eight hours when intensive treatment has been given. In the average case, improvement begins after twenty-four to forty-eight hours. A return of symptoms means regeneration of the thymus and indicates further treatment. In the writer's clinic, the treatment is as follows: Exposure with the central ray is made directly over the middle portion of the thymic region, anteriorly and posteriorly, for five minutes each, with a 9-inch spark gap 5 ma., 9-inch distance with 3 mm. aluminum and sole leather filter. Three successive treatments at ten-day intervals are given, unless more frequent treatment is indicated.

Radium Therapy.—Satisfactory results have been reported from the use of radium. The technic used has been cross-firing with 100 mg. of radium element filtered through 0.5 mm. of silver at ½-inch skin distance. Four portals of entry are used. Radiations are made over the anterior aspect of the chest, directly over the thymus, lasting two hours at each portal, a total of 800 mg. dosage. When more intense radiation is required, 200 mg. may be used with half the time exposure.

Preventive Treatment.—The thymus gland in about 50 per cent of otherwise normal children is sufficiently large to be made out by percussion and to cast a shadow in the roentgenogram. The question has already arisen as to the advisability of employing preventive treatment in these patients in the absence of thymic symptoms. Whether roentgenization or radium should be employed in all patients with an enlarged thymus, unassociated with clinical symptoms, cannot be answered positively at the present time. It would seem advisable, however, to urge the use of preventive roentgenization or radiation in selected cases and prior to anesthesia, as its use has not been followed by any ill effects.

Treatment of Tumors and Syphilis.—The treatment of benign (lipoma, myxoma, fibroma, dermoid cysts) and malignant (carcinoma, lymphosarcoma, sarcoma) new growths, tuberculosis, syphilis and other affections of the thymus, differs in no particular from the treatment employed when the process develops in other organs or tissues.

REFERENCES

Benjamin, J., and Lange, S. Arch. Pediat., xxxv, 1918.

Blackfan, K. D., and Little, C. Am. Journ. Dis. Child., xxii, 459-470, 1921.

Crotti, A. Thyroid and Thymus, 2d ed., 1922.

Friedlander, A. Arch. Pediat., xxviii, 1911.

——— Am. Journ. Dis. Child., vi, 38-56, 1913.

Hammar, J. A. Arch. f. Anat., 1906.
Heinecke, L. München. med. Wchnschr., L, 2090, 1903.
Heublien, A. C. Am. Journ. Roentgenol., vii, 191, 1920.
Hoskins, E. R. Endocrinology, ii, 241, 1918.
Klose, H. Verhandl. d. deutsch. Gesellsch. f. Chir., xxxix, 379, 1910.
——— Arch. f. klin. Chir., xcii, 1125, 1919.
Klose, H., and Vogt, H. Beitr. z. klin. Chir., lxix, 1, 1910.
Lange, S. Am. Journ. Roentgenol., lxi, 556, 1913.
MacCallum. Textbook of Pathology, 2d ed., 1920.
Matti, H. Ergebn. d. inn. Med. u. Kinderh., x, 1, 1913.
Noback, G. J. Am. Journ. Dis. Child., xxii, 120, 1921.
Pappenheimen. Journ. Exper. Med., xx, 477, 1914.
Park. Am. Journ. Dis. Child., xviii, 317-512, 1919.

CHAPTER XIV

DISEASES OF THE PITUITARY GLAND
(*Hypophysis Cerebri*)

WILLIAM N. BERKELEY

Anatomy.—The anatomical relations of the pituitary gland, its two parts, its infundibular process (stalk), and its peculiar site in the sella Turcica or pituitary fossa at the base of the skull are fully described in the textbooks of anatomy.

Histology.—The histology of the anterior part of the gland, with its vascular and nervous supply, is in general that of the other glands of internal secretion. The *pars intermedia,* the supposed secreting part of the posterior gland, is different in that it is thought to discharge its secretion, at least in part, not into the veins and lymphatics but directly into the cerebral ventricles.

The accepted *clinical theory* of pituitary disease rests largely on the laborious and classic work of Cushing and his associates. The recent publications of Camus and Roussy, and especially of Bailey and Bremer, offering evidence that minute lesions of the *tuber cinereum,* in the brain itself, just above the pituitary, will produce diabetes insipidus and Froelich's disease (see page 169) with a perfectly intact pituitary gland, require further confirmation. Cushing himself, while preserving an open mind, still seems to believe that the accepted views are more tenable.

PITUITARY DISEASE

Inflammations.—Inflammations are possible but rare. Tuberculosis, gumma, and septic and other forms of meningitis may involve the gland. When the diagnosis can be made, treatment should be directed toward the relief of the primary trouble.

Calcification.—Calcification, with signs of hypofunction, has been recently described by Pfahler and Pitfield. The diagnosis is to be made, according to these authors, by the appearance of unusual shadows at the margins and in the hollow of the sella. Gland therapy was of benefit in

one instance, where the trouble (of many years' standing) was supposed to have followed chronic sphenoidal sinusitis. The patient's most annoying symptom, persistent sleepiness, was entirely relieved.

Tumors of the Pituitary Gland

Cysts, fibrosis, and various cellular tumors are observed. "Hyperplasias" and adenomata of the anterior body, growing slowly, may erode or bulge the bony walls of the sella, or spread laterally before penetrating the dural covering and invading the brain. Bony growths in the neighborhood of the sella, and tumors of other parts of the brain, may indirectly or directly compress the gland, or obstruct its circulation. Cysts and cellular tumors of the stalk also occur.

Symptomatology and Diagnosis.—The symptoms may be only those of intracranial pressure, headache, vomiting, choked disc, and epileptoid convulsions. Severe bitemporal headache is emphasised by Cushing as an early sign. The special signs of tumor at the base of the brain are also observable, and there may be narrowed fields of vision and primary optic atrophy before choked disc occurs. Various palsies of the external muscles of the eye have been noted. Mental disturbances of many kinds occur in adults, and in children mental retardation and idiocy are at times observed. Besides signs of pressure and tumor, *dyspituitarism* (see page 166) is common, and upon this most often an accurate localizing diagnosis can be made.

Roentgen Rays—*Roentgenograms,* which seem first to have been suggested by Oppenheim as an aid to the diagnosis of pituitary tumors, are almost indispensable. Profile plates and films, both direct and stereoscopic, from several different angles, may be needed. The clinoid processes and walls of the sella may appear thickened (acromegaly), or thinned, distended ("ausbuchtet," Oppenheim), eroded, partially absorbed, or completely destroyed. The interpretation of the photographs is not always easy. The size and shape of the normal sella are quite variable. L. G. Cole recently showed me a sella 14 by 15 mm. in size, from a mentally gifted and physically normal man of medium height, whose head was X-rayed for another purpose. All readings should be conservative, and carefully correlated with the other signs of the suspected condition. Serial radiograms may show growth or recession of a tumor.

Treatment.—Since Horsley's experimental extirpations in animals in 1886 surgical methods of attack have been slowly perfected. The technic and relative advantages of the trans-sphenoidal and subtemporal operations are fully treated in the textbooks of surgery. Surgical methods may be used for decompression, for the relief of neighborhood symptoms, for draining pituitary cysts, or for reducing the output of a hyperfunctioning anterior lobe by partial excision (Cushing).

X-ray therapy of pituitary tumors is at times a valuable adjuvant of surgical methods. Relief of headache and enlargement of previously restricted fields of vision are useful clinical guides to the amount of irradiation that may be needed. Dosage and the length of intervals between sittings must be adjusted to the individual case. Blumberg recently writes optimistically of this procedure.

Secretory Disorders of the Pituitary Gland (*Dyspituitarism*)

Physiology.—The *physiology of the pituitary* is a subject in which much confusion still prevails. If the work of Bailey and Bremer be generally corroborated, all the current conceptions must be revised. At the present time the prevailing view still is that the *anterior lobe* is intimately concerned with growth and the development of the long bones. But after growth is completed, and the shafts and epiphyses of the long bones have united, the anterior lobe is still in some unknown way essential to life. Complete removal in animals is soon followed by tremors and twitching of the muscles, arrested appetite and digestion, coldness, coma, and death. Death occurs in a day or in a few days, the longer period seeming to coincide with accidental failure to remove all remnants of the gland. Paulesco, in his monograph, and Cushing have reported this result in a very large number of experimental operations.

When part of the anterior lobe is left in a viable condition, and the *posterior lobe,* or its secreting portion (pars intermedia) is cut away, leaving the upper end of the stalk, the animal survives, but grows fat (increased carbohydrate tolerance), has a lowered temperature and blood-pressure, and shows partial sexual involution, or, if a puppy, fails to develop the sex glands. Atrophic changes in the skin and hair may be noted, and the quantity of urine is often greatly increased. In puppies the intelligence is clouded. In view of this multitude of diverse symptoms it seems unlikely that only a single secretory principle is produced either by the anterior or posterior parts of the gland, but of this nothing is now known.

Clinical Types of Secretory Disorders

Hyperpituitarism or Acromegalia.—*Hyperpituitarism of the anterior lobe* has for its typical clinical form the curious disease first described by Marie in 1886 as "acromegalie" (enlargement of the extremities). Marie himself believed the pituitary body to be functionally deficient in this disease. Most subsequent writers have judged it to be overactive.

Symptoms.—Both sexes are affected. The disease begins most commonly in the third decade. Hands and feet are greatly enlarged, both

bones and soft tissues being involved. The nails are broad. Head and face increase in volume. Upper and lower maxillæ often grow so much as to leave spaces between the teeth, such as appear between the milk teeth of rapidly growing children four and five years of age. The ears may be enormous. The chest and spine may be involved later on, with pronounced kyphosis. Menstruation is apt to be suppressed, and in men impotence is common. Local symptoms from the enlarged pituitary gland include primary optic atrophy, headache, somnolence and stupor.

Course.—The course of the disease varies with the causation. The disease may progress for some months or years and terminate fatally. Again in other cases rather rapid progress for a time is followed by remission of all the symptoms, or even by hypopituitarism. The condition is thus at times analogous to the hypothyroid state, often resulting after a long attack of Graves' disease. The mind may be entirely unaffected for a long time, and the patient can go about his daily tasks as usual.

When a hyperpituitary condition develops in childhood, the same general sequence of symptoms appears, with the difference that the long bones grow abnormally fast, and *gigantism* is produced. Osler states that "the skulls of some notable giants show enormous enlargement of the sella Turcica."

Diagnosis.—The diagnosis should be based upon the symptoms, history and X-ray photographs. Certain cases of osteitis deformans, of hypertrophic pulmonary osteo-arthropathy, and of syringomyelia are said to be at times very similar in appearance; but mistakes do not appear to be common.

Treatment.—In case of tumor the treatment should be that already described for tumors. Results of operation are variable. A very discouraging report of four operations on pituitary adenoma has been recently made by Hunter. Cushing's results have been more promising. Therapeutic X-ray exposures may diminish the glandular output and reduce the size of the growth.

Cases treated expectantly sometimes do well. If a hypopituitary condition finally supervenes, pituitary gland may be given. The general condition and feelings of the patient are said to be often relieved by such medication, though the skeletal enlargement is, of course, permanent. The result is here again analogous to the permanent thyroid struma, "popped" eyes, and damaged heart in spent cases of exophthalmic goiter.

Hyperpituitarism of the posterior lobe, as an uncomplicated clinical entity, is unknown, so far as I am aware. It might be found as a temporary antecedent of Froelich's disease (see below), but that the cases are not seen in time. I have reported one case which might be so classified, but in view of the insufficient data the diagnosis would be subjective only. Theoretically, the symptoms would be emaciation, high blood-pressure, glycosuria, and diminished urinary output. Perhaps some cases of sup-

posed "pituitary" glycosuria belong here; but fractures of the skull, blows on the head, and various lesions at the base of the brain will present at times the same phenomenon.

Hypopituitarism.—*Hypopituitarism of the anterior lobe* has already been alluded to as an occasional terminal condition in acromegalia, sometimes symptomatically benefited by opotherapy. When primary deficiency is associated with tumors and cysts of the gland, operative interference may be considered.

Primary anterior lobe deficiencies of a "functional" or at least of a temporary and curable character, may be suspected in boys and girls of the "infantile" type, in whom a complete examination carefully and repeatedly made is negative for any organic lesion in the brain and sella, and in whom the mentality is not deficient nor the thyroid gland at fault. A long series of New York Public School children of this character have passed through my hands at the Good Samaritan Dispensary in the last fifteen years. They receive whole pituitary in suitable doses, and in the course of one or two years they grow remarkably, to the delight and admiration of themselves and all their family connection. One small boy of fourteen years, stationary for four years previously, grew nearly 10 inches in the year after treatment was begun, and developed all the external signs of puberty. He was a bright and attractive boy otherwise, a monitor at school, and a favorite with teachers and comrades. He was a half head shorter than a normal younger brother of twelve, when the treatment was begun.

Such diagnoses are confessedly only clinical guesses. The old fallacy, *post hoc, ergo propter hoc,* is not excluded. But frequent repetitions of such an experience increase one's confidence that a correct diagnosis has been made. The "lame" anterior gland, after use of the therapeutic "crutch" for a few months or years, is able to walk alone again. The same thing happens in minor grades of hypothyroidism after giving thyroid.

One remarkable case of a boy of seventeen who had made good progress through the grades, but was falling behind at high school, illustrates the negative side of the last paragraph. He was very small, had not grown any since his tenth year. He was also pale and thin, and had a piping voice, and a curious senile look, accentuated by small wrinkles at the outer angles of the eyes. The mentality was good. He wore glasses but the eye backgrounds were reported normal by a very competent oculist. The physical examination and the urine were negative. He had no headache, and no history of fits. Pituitary failed to do him any good, and he one day very unexpectedly had a fit, and two days later another; in the latter he died. The autopsy showed a moderate-sized tumor of the pituitary stalk. This case might be symptomatically compared in some ways with the curious *progeria* of Hastings Gilford, though it has also relations with the "Lorain" type of infantilism.

Symptoms of *hypopituitarism of the posterior lobe* (*Froelich's disease*) affecting only the pars intermedia depend mainly upon the increased carbohydrate tolerance, and the involution of the sex organs. Clinically the condition is not very unusual. It is commonly known as the "Froelich syndrome," or *dystrophia adiposogenitalis*. Froelich described the first cases in 1901. The patient is sometimes a monster of fatness, and is able to take much more than 100 gm. of glucose without glycosuria. The blood-pressure is often lowered. Impotence in men and amenorrhea in women are to be expected. In children the gonad glands remain undeveloped, and in boys the prostate (Lisser) is often found rudimentary.

Associated with this condition, but sometimes occurring as an isolated symptom, is *diabetes insipidus*. The symptoms are well known and do not require special comment. So far as my own records go, there is no increase or decrease in the blood-sugar, and the very light urine, passed in enormous quantities, never contains even a trace of glucose. As a clinical phenomenon of unknown causation, the disorder has been known to physicians for years. From present available evidence it seems probable that a majority of the cases are due to posterior pituitary deficit, though this is disputed by Bailey and Bremer. The prognosis is not always good as regards permanent cure of the trouble, though life may be indefinitely prolonged.

Treatment.—In uncomplicated posterior lobe deficiencies a rational treatment would consist in simply administering posterior gland. Such treatment is sometimes of considerable benefit, but recovery will depend upon the cause. This must be diligently sought in each case. Circulatory ("functional") insufficiency is only to be presumed when X-rays are entirely negative, and a close study of the case in other respects shows nothing amiss. Syphilis, tumors of the gland and stalk, even indirect intracranial pressure transmitted from distant parts of the brain may be at the root of the trouble. Three times in subacute "Froelich" cases I have noted a very shallow fossa overhung by thickened and *overlapping* anterior and posterior clinoids. No prognosis should be given unless a cause can be located.

Large doses of thyroid given to the point of tolerance and combined or not combined with posterior pituitary gland may help to reduce the fat and develop or restore the genitals. In adults the basal metabolic rate should be determined before thyroid is given; but the B.M.R. in pituitary disease is said to be unreliable as an indication of thyroid activity.

Diabetes insipidus, whether a part of the complex or a single symptom, appears pretty generally to be temporarily relieved by hypodermic injections of small amounts of any of the commercial posterior lobe extracts. The dose depends upon the gravity of the symptoms and the weight of the patient. Usually 0.5 c.c., or less, is an effective dose for average cases. Barker and Mosenthal, Blumgart and others have reported suc-

cessful medication of this kind. It is, however, not often practicable to continue such daily injections. Blumgart in 4 cases found that the condition could be relieved temporarily as well by *intranasal spraying* of pituitary extract as by hypodermic injection; but larger doses were required. Pituitrin "O" (Parke, Davis and Co.) was the drug used. Five cubic centimeters was the maximum amount used at one time as a spray.

A careful study of the X-ray films and cerebral signs should be made with a view to possible location of a cause. The Wassermann reaction should never be omitted. In an enormously fat idiot boy of eight years, now in my care, polyuria has been an annoying and constant symptom; but the profile X-ray films of the skull have been entirely negative, the retinæ are negative, and there has been no headache or other sign of definite increase in intracranial pressure. One cannot even guess at the precise lesion.

Clinical reports of *oral administration* of pituitary preparations for diabetes insipidus are mostly negative; but as no information as to the nature of the extract employed is usually given, such reports are of little value. A properly prepared extract is a *sine qua non* to start with, and such a preparation ought to act at least as well as the "fresh glands" which are occasionally mentioned in the literature as being effective by the mouth (see remarks under Administration, page 171). I have had excellent results from the oral use of pars intermedia properly made, and in doses of a few tablets a day.

A note should be added on the subject of *acute surgical apituitarism.* It develops sometimes after surgical operations and threatens the life of the patient. In the absence of hypodermic preparations representing the whole gland, and in view of the doubtful absorptive capacity of the stomach, Cushing has successfully tried *gland transplantation* into the cortex of one patient so affected. The gland was taken from the skull of a newborn babe dying of hemorrhage.

The question of grafting glands is a difficult one. Many more data from competent sources must be collected before the question is settled. Halsted's view is that a "physiological deficit" must exist to insure a "take." See the note on parathyroid grafts in tetany (page 146) for other details.

Mixed Forms of Dyspituitarism

Symptomatology and Diagnosis.—The clinical symptomatology and diagnosis of these cases involves many difficulties. In the absence of facts, medical imagination has run riot.

Theoretically we may have four forms. Calling the anterior gland A, and the posterior gland P, we may have:

A plus and P mini
A plus and P plus
A minus and P minus
A minus and P plus

When we add that each plus element may in time become normal or minus, and that the effects of any temporarily active condition often persist after the cause has ceased to operate, we may well cry in the words of scripture, "Such knowledge is too wonderful for me; I cannot attain unto it." In obscure pituitary cases I think this a good scientific frame of mind to cultivate. Clinical histories and autopsy reports are still to be collected and studied in large numbers before diagnosis in many of the cases can be anything but premature and unauthorized assumption.

Medical literature at present is full of curious "pituitary" cases ingeniously interpreted by ingenious physicians. Epilepsy, petit mal, functional sleepiness, fainting fits, menstrual headaches, migraine, and dozens of other troublesome and obscure disorders are said to be instantly cured by giving "pituitary gland." By the thoughtful reader of such reports only the Scotch verdict, "not proven," can be handed down.

Many mixed cases seem complicated also by thyroid, gonad, and adrenal dyscrasias ("pluriglandular" conditions), and often the conscientious observer must frankly avow that an exact diagnosis is impossible.

Treatment of Mixed Cases.—The treatment should therefore be based upon the more obvious clinical indications. These have been sufficiently set forth already. No hard and fast rules can be given. Fortunately the mixed cases are not very common. And when they appear, as they most frequently do, in congenital brain disease of various organic types, treatment is useless, and the diagnosis is only a matter for academic discussion.

Administration of Pituitary Gland

Bullock's glands are those generally used for therapeutic purposes. Possibly bulls and cows only should be used in order to avoid the effect on the pituitary supposed to be produced by castration. I know of no serious researches, however, in which this matter has been experimentally tested.

Extracts.—Robertson has claimed that a lipoid of therapeutic value can be extracted from the anterior lobe. He has called this extract *tethelin.* Subsequent experiences do not seem to have confirmed this work. The only known posterior lobe extract, gotten by a rather complicated process, involving prolonged boiling, and sold under various trade names (pituitrin, infundibulin, etc.) is of value for its drug effect as a blood-pressure stimulant and oxytocic. It may be, possibly is, one normal constituent of the gland, but it would be highly premature to affirm that the function of the pars posterior is limited to this substance.

In view of these obvious difficulties both fresh and frozen glands have been used, and not only by the mouth, but in suspension as a hypodermic injection. Freezing the glands, in my opinion, only invites decomposition and autolysis, and even with fresh glands the method is crude, inaccurate, and uncertain.

The least objectionable recourse at present is *fresh whole gland,* anterior and posterior, mixed or separate as occasion may require, dried rapidly in the cold, pulverized, and entirely untreated with any fat solvent. Some New York dealers now make such preparations, and attempt no standardization except *weight*—so much dried powder being equivalent to so much fresh gland. Kjeldahl nitrogen determinations are fruitless so long as we do not know how much nitrogen, if any, a perfect extract ought to contain.

When the oral administration of dry extracts fails, *hypodermic preparations* must be considered. As little or nothing is known of pituitary lipoids, the best recourse is a nucleoprotein precipitate of the part of the gland required, redissolved quantitatively and after Berkefeld filtration stored in sealed ampules. In an emergency a faintly alkaline saline solution of the fresh glands may be used after Berkefeld filtration. Autolytic processes may cloud it, however, in a few days.

Dosage.—The commercial extracts vary in potency. Many are probably entirely inert. Cushing and his associates describe the administration of enormous doses of dried pituitary by the mouth, 100 gr. or more per day. Inasmuch as the entire fresh pituitary gland (four-fifths water) of a 2,000-pound bullock weighs only 20 to 40 gr., and the fresh pars intermedia only 2 to 4 gr., we can only presume that in such cases the material was inert, or that absorption was precluded by the condition of the patient's alimentary tract. When the preparations are made as I have above suggested, a few grains a day in split doses is usually enough to begin with. Much larger amounts may, however, be given without danger when the case is urgent, or when smaller doses have failed. There is, I think, no question that pituitary material of the kind mentioned, when given by the mouth, is therapeutically active and efficient.

The dose of the hypodermic preparations is tentative, and is to be controlled by the needs of the patient and the progress of the disease. I know of no fatalities from overadministration, unless mention be made of the obstetric accidents indirectly due to the careless use of commercial posterior lobe extract.

REFERENCES

Bailey and Bremer. Arch. Int. Med., xxviii, 773, 1921.
Barker and Mosenthal. Journ. Urol., 449, 1917.
Berkeley, W. N. Med. Rec., Oct. 8, 1921.

Blumberg. München. med. Wchnschr., lxix, 739, 1922.
Blumgart, H. L. Arch. Int. Med., xxix, 508, 1922.
Cushing, H. The Pituitary Gland and Its Disorders, J. B. Lippincott Co., Philadelphia, 1913.
——— Journ. Am. Med. Ass., lxxvi, 1721, 1921.
Froelich, A. Wien. klin. Rundschau, xv, 883, 1901.
Gilford, Hastings. Practitioner, 1915.
Hunter, J. W., Jr., Virginia Med. Month., Jan., 1922.
Lisser, H. Endocrinology, Jan., 1922.
Oppenheim. Arch. f. Psychiat., xxxiv, 303, 1901.
Paulesco, N. C. L'Hypophyse du Cerveau, Paris, Vigot Frères, 1908.
Pfahler and Pitfield. Am. Journ. Med. Sc., April, 1922.
Robertson, T. Brailsford. Journ. Biol. Chem., 1916.

CHAPTER XV

DISEASES OF THE PINEAL GLAND

WILLIAM N. BERKELEY

TUMORS AND INFLAMMATIONS

Somewhat less than a hundred tumors of the pineal gland (epiphysis cerebri, conarium, Zirbeldrüse) have been reported. One was syphilitic; one was a large tubercle. Cysts, teratomata, and cellular tumors are also on record; the last variously and rather subjectively classified. "Brain sand" can hardly be called a pathological condition. It may appear in the pineal body at any age, just as it does in the choroid plexus (S. Vincent).

Symptoms and Diagnosis.—The symptoms of pineal tumor are those of new growth in the mesencephalon, headache, vomiting, strabismus, choked disc, and convulsions. In children under puberty there is sometimes, in addition, a remarkable increase in growth, with precocious mental and sexual development (see below). In these cases the clinical diagnosis has been successfully made. In adults it is often much more doubtful, though Dandy believes that careful study will minimize clinical errors. Lereboullet believes that a condition present in two cases reported by himself, *paralysie verticale du regard* (inability to turn the eyes upward), is a valuable diagnostic sign of growths in the region of the corpora quadrigemina. The Wassermann test should, of course, be made. If there is any "sand" or "lime" in the gland, it may be often identified by shadows in profile X-ray films about 1 cm. behind and 3.5 cm. above the external auditory meatus (Schüller).

Treatment.—The treatment is always surgical except in the case of lues. Dandy has devised an operation for pinealectomy in man. He reports three cases. In one the growth proved to be infiltrating, and was not removed. In a second (tubercle) the growth was successfully removed, and the patient lived eight months. There were no unfavorable mental or physical effects from operative injury to the brain. A third case survived forty-eight hours—dying probably of causes not attributable directly to the excision of the tumor.

SECRETORY DISORDERS

The view was advanced in the last century that the pineal gland is only a vestigium of a third eye, occipitally situated, and still observable in certain reptiles and fishes. Whatever may be its evolutionary relation, the opinion is gaining ground among clinicians that physiologically in higher mammals it is a true organ of internal secretion. Supporting this conception there are both experimental and clinical data, but the question is still *sub judice*. A brief statement of the evidence is all that is now justified. Premature and violent conclusions do nothing but harm.

Modern interest in the pineal gland as an organ of internal secretion dates back only about fifteen or twenty years. In 1909, von Hochwart reported a tumor of the pineal gland in a boy of five years. Besides the usual signs of brain tumor, the child showed a physical and mental precocity far beyond his years. He was as large as a boy of nine years, had a bass voice, large genitals, and well grown pubic hair, and he concerned himself with ethical problems and immortality.

Von Hochwart's case has not remained isolated. A series of tumors of the pineal gland in children has been reported or collected. Horrax gives a good bibliography, which has been completed by Zandrén in foreign and American literature since that date. The symptomatology has been often (not always) strikingly uniform, and nowadays signs of brain tumor in the region of the corpora quadrigemina in children under puberty, concurrent with abnormal growth, early development of pubic hair, and sexual and mental precocity, are grouped definitely as the "pineal syndrome" (*macrogenitosomia præcox*). A smaller number of pineal cases have shown excessive adiposity only ("cerebral adiposity").

The autopsy on von Hochwart's case, which may be taken as a type, showed a mixed tumor (teratoma) of the pineal gland. So far the facts are admitted. Explanations, however, have varied. Mechanical compression of the pituitary, informally suggested by Cushing, fits well as an explanation of the rarer cases in which adiposity has been the only extracerebral sign; but it entirely fails to explain the typical syndrome. Von Hochwart and Marburg thought it necessary to assume that the tumor destroys the gland. In consequence the normal gland must inhibit growth and sex development. Askanazy believed the explanation to lie in the teratomatous nature of the tumors, testis and ovary being presumably present, and secreting as elsewhere; but not all the typical cases were teratomata. Dana thought it possible that the tumor often (the histology being variable in the different cases) might *reënforce the gland,* exaggerating the normal effect of the pineal secretion. Pineal tumors would then often act as thyroid tumors and pituitary tumors often do. Dana and Berkeley working upon the question for several years without prejudice

(with some assistance kindly extended by the Trustees of the Rockefeller Institute) reported that perfectly fresh pineal gland from calves and young cattle hastened the growth of kittens and young rabbits and guinea-pigs to a marked degree, as compared with suitable controls. A number of backward children, without visible organic stigmata, to whom the gland was given for a period of three months or more, made an advance in mental age considerably in excess of any previous progress for a like period.

About 50 children were treated. Twenty-one at the Vineland, New Jersey, Training School, were in the care of Goddard and Cornell. Fourteen of these in four months made twice the normal mental development. The remaining 29 were mostly referred to my Clinic from ungraded classes in the New York public schools. Goddard some years later inclined to the view that the administration of pineal gland had not benefited his pupils at Vineland; but most of the cases in my care were definitely improved. I append, as an example, the clinical notes on the case of B. W., a boy of 11, who was treated from June to August, 1911.

Case 21.—Benny W., New York (Dr. Berkeley). Weight 42½ pounds; height, 43½ inches; age, 7 years. Family history: Father not seen, but reported healthy; age not ascertained. Mother, 33 years old, of excellent appearance. There are three other children, all boys, aged 13, 11 and 5 years respectively; all these were seen, and all were normal, or even precocious. Date of first visit, June 15, 1911. Personal history: Child born without incident, but was always backward. Did not walk till three, and has never said any connected or intelligent words. He can repeat short sentences after his mother, but this appears to be true echolalia, as he gives little appearance of understanding what he repeats. Cannot buy a pennyworth of candy. Is said to wet himself habitually, and soils himself several times a week. Mother professed herself in despair about the child and willing to do anything for his relief. Physical examination entirely negative, except that the boy is cross-eyed (1.50 D. hyperopic astigmatism). He has no physical stigmata, but presents a vacant animal face, smiles inanely and drools continually. His muscles and skin are relaxed, and he stands with bent knees and bowed head. He is said to be very "nervous," and cries a good deal, which might be attributed to the quantity of coffee he has been allowed to have. The treatment of this case consisted solely in the giving of pineal gland. His eyes were fitted with glasses, but these he soon refused to wear, and the treatment was continued without them. June 26.—Weight 43¼ pounds. Looks brighter. Mother thinks his mental condition much improved. Has gone to toilet alone and not soiled himself at all this week. Has said some connected words; cried because younger brother was dressed before him (had never noticed this before). July 3.—Mentality still improving; talks a great deal more. Weight, 41¾ pounds—a decline due possibly to

the hot weather. July 10.—Weight, 42 pounds; intelligence rapidly increasing; yesterday asked his mother for the key to the toilet; has entirely ceased to soil or wet himself. Height unchanged. Nurse and assistant at the Clinic remarked upon the patient's improved appearance. August 14.—Weight, 44¼ pounds; height 44½ inches. Understands and answers simple questions, and has acquired between fifty and one hundred words. Facial expression transformed. Habits entirely correct. This patient continued to improve till late August, when the family moved suddenly to a western city and were lost sight of.

Sisson and Finney, and Hoskins, working with rats, were unable to confirm our animal feeding experiments, but McCord fully confirmed and amplified them, and Zandrén seems to have strengthened the chain of positive evidence by reporting a remarkable case of a boy of sixteen and one-half years without a pineal gland, apparently a genuine case of apinealism. This boy was a moron, there having been no growth nor mental development since he was ten years old.

Zandrén inclines to the belief that the pinealectomy experiments so far published (Foa, Sarteschi, Dandy, Horrax), which are apparently in contravention of this view, are objectionable as evidence, being either conflicting in their results with one another, imperfectly controlled, or done upon animals too far down in the zoölogical scale to be fairly comparable.

The data above summarized seem to justify at least the *provisional* conclusion that the pineal gland in many of the higher mammals speeds up the chemistry of growth, and hastens the appearance of puberty.

Timme has suggested that "progressive muscular dystrophy is an endocrine disease, and that the pineal gland is the organ at fault in such cases." His argument is based partly upon clinical signs, partly upon the appearance of pineal shadows (see above) in the X-ray pictures of the skulls of the patients too young for calcification to have developed. I have not found any confirmation of this suggestion in the literature.

Treatment of Secretory Disorders.—The principles of treatment may be inferred from the foregoing discussion. For *hyperpinealism* see Tumors (p. 175). Definite anatomical *apinealism* is only a clinical curiosity. *Hypopinealism* in adults has not been identified, but in early childhood it manifests itself as a simple retardation of bodily growth and mental development, and is usefully treated with gland extract. While the case described was unusually successful, many backward children in my care have done remarkably well on the treatment. In the care of all such cases one should continually bear in mind that "mental backwardness" in a child is a vague term covering a multitude of unknown conditions. A careful and minute examination of every feature of each case must be repeatedly made. Outside of the cretins and Mongols but few generalizations are possible. The prenatal history is important; the character of

the labor, and the infant's nutrition and food must be carefully looked into. The mental age must be accurately determined. The special senses, the tonsils and adenoids, the teeth (both present condition and stage of eruption), the skin, the blood-pressure, the shape of the hands and feet, the quality and distribution of the hair, the relation of the weight and height to the age, are all of prime importance. X-ray photographs of the skull showing the pituitary fossa and giving possible indications of pressure, or of cysts, neoplasms, or hemorrhages of the brain, are almost indispensable. A serological examination of the spinal fluid should be a routine measure.

When all this work has been carefully done, it will soon become evident to the careful and attentive student that glandular deficiencies often do not come singly, and pineal gland must not infrequently be combined with other secretions. Minor grades of hypothyroidism especially should be suspected. A dry skin, cold extremities, obstinate constipation, excessive mental hebetude, irregular and imperfect eruption of the milk teeth, low blood-pressure, one or many of these conditions may be intractable till thyroid is added to the formula. When there are very marked anomalies of physical growth, with changes in the size of the sella, or increased carbohydrate tolerance, great obesity, or a systolic blood-pressure below 50 mm., the anterior or middle or whole pituitary should be added. When the patient is a boy, and has minute and soft testes (a common occurrence), testis should be given. Sometimes several of these conditions coincide, and a pluriglandular formula should be tried. The results are often gratifying.

A warning note should be added as to the material used in filling prescriptions for pluriglandular compounds. One young medical friend telling me recently of his ill success in a certain case said he had sent the patient's mother to the nearest pharmacy, directing the pharmacist to "use the very best materials he had." This is like asking the milkman's advice in making up a formula for a baby with chronic diarrhea. There are now several dealers who specialize in pluriglandular formulas; and if the medical attendant hopes for results in any measure commensurate with his thought and effort, he should be sure that his medicament is fresh and reliable.

Administration of Pineal Gland.—I prefer a physiologically standardized dose. Twelve perfectly fresh glands from young bullocks, or twice that number from calves, are dried rapidly in the cold with a convenient amount of milk sugar and made into 100 capsules or tablets. Each dose thus made corresponds roughly to about 70 kg. (150 pounds) of live animal. The tablets are not toxic, but 2 or 3 a day seem to be enough for small children. In sucklings the dose may be mixed with the milk. McCord has devised an ingenious method of standardizing the gland by noting its action on the pigment cells of the tadpole. Small doses fre-

quently repeated and continued over long periods of time give the best results. By "long periods of time" I mean not weeks and months, but years.

REFERENCES

Dana, C. L., and Berkeley, W. N. Med. Rec., lxxxiii, 835, 1913.
Dandy, W. E. Surg., Gynec. & Obst., xxxiii, 113, 1921.
Hochwart, F. von. Deutsche Ztschr. f. Nervenh., 1909.
Horrax, G. Arch. Int. Med., xvii, 607, 1916.
Hoskins, R. G. Journ. Exper. Zoöl., 1916.
Lereboullet. Progrès Méd., xxxvii, 75-77, 1922.
McCord, C. P. Journ. Am. Med. Ass., July 18, 1914, and later publications, same journal.
Schüller, A. Deutsche Ztschr. f. Nervenh., i, 188, 1913-1914.
Sisson and Finney. Journ. Exper. Med., 1920.
Timme, W. Arch. Int. Med., Jan., 1917.
——— Tr. N. Y. Neurol. Soc., 1918.
Vincent, S. Internal Secretion and Ductless Glands, 2d ed., Longmans, Green & Co., New York, 1922.
Zandrén, S. Acta Med. Scandinavica, liv, 1920-1921.

CHAPTER XVI

DISEASES OF THE GONADS

WALTER TIMME

DISEASES OF THE MALE GONADS

There is no room here for an exposition of the anatomy, embryology, histology, physiology, comparative anatomy and allied subjects which bear upon this topic. Granted their importance to the intelligent diagnosis and treatment of the testicular diseases, we must content ourselves with only the larger aspects of these sciences as they relate to the matter at hand.

Functions.—Aside from the function of spermatogenesis, the testes are now generally credited with an internal secretion. The evidence in support of this view is voluminous and compelling. The effect of castration in mammals as well as human beings is a matter of common knowledge. Perhaps the most striking experimental evidence is that of Steinach and Sand, who successfully grafted the ovaries of guinea pigs into previously castrated males, thus producing "feminized males" who developed characters peculiar to the female. Likewise they reversed the process and produced "masculinized females." Such experiments as these leave the protagonists of the old nervous control mechanism theory little ground to stand on, and, further, almost completely delimit the nature of the influence of the gonads upon the development of somatic sex characteristics to an endocrine factor. The cells which fill the interstices between the seminferous tubules, and which were first described by Leydig (interstitial cells of Leydig), have been singled out as the elaborators of this incretory element. Embryologically, they are different from the spermatogenic cells (Bouin and Ancel, Chapin, Allen, Whitehead and Felix). These cells show periodic activity synchronous with the rutting season in animals (Marshall, Le Callion, Watson, von Hansemann and Rasmussen). Histologically they are of secretory character (Cowdry). Experimentally, the germ cells have been found to atrophy following exposure to X-ray and also after vasectomy, while the interstitial cells remain intact, yet the stigmata of sex remain unaltered in these cases (Regaud and Dubreuil, Wheelon).

Hypersecretion

Precocious Puberty.—This condition variously known as pubertas præcox, macrogenitosomia præcox and precocious puberty is one in which the secondary characteristics of sex appear before the usual age of puberty. This may occur at any time from birth to the age of twelve or thirteen years. There is increase in the size of the penis and testicles with evidence of function such as erections, pollutions and frequently masturbation. Hair appears on the pubis, in the axilla and on the face; muscular development tends to the adult type and growth is usually retarded. Behavioristically these children are difficult to control and show a great fondness for embracing the opposite sex; there is often a tendency to exhibitionism. This condition must be differentiated from virilismus and hirsutismus. The former shows the adult hair distribution and the latter a general bodily hypertrichosis, but neither show evidences of gonadal function.

While pubertas præcox is undoubtedly an endocrine disturbance in which the gonadal secretion is predominately affected, yet the primary pathology is often elsewhere. Cases are described in which the pineal, pituitary, suprarenal cortex and testes are each separately held responsible for the development of this condition; hence it is necessary to discuss this subject under each of these headings.

The Pineal Type.—Most of the cases of this class have been reported in connection with tumors of the pineal body revealed at autopsy or following operation. Intracranial pathology caused by the expanding tumor mass complicates the picture and therapy is of little or no avail. In spite of conflicting experimental evidence as to whether the sexual precocity is due to an oversecretion or undersecretion of the pineal, the feeding of this gland has been found helpful in certain cases of precocity not associated with tumor, but in which a pineal shadow in the X-ray and associated muscular asthenia pointed to an epiphyseal deficiency (Timme). The dosage is pineal substance desiccated gland, gr. $\frac{1}{5}$, twice daily, after meals.

The Pituitary Type.—Cases of this type are rare. The only reported cases are in the female and they will be discussed in the section on the female gonads.

The Suprarenal Cortex Type.—The development of the testes and suprarenal cortex from the same embryological structure, namely, the wolffian ridge, would seem to predicate a close relation between these two glands. Experimentally, R. G. and A. D. Hoskins produced gonadal hypertrophy in white rats by feeding suprarenal cortex. Further evidence is furnished by the numerous reported cases of pubertas præcox associated with hypernephroma (Jump and Lespinasse). The diagnosis in these tumor cases is usually made by palpation of a tumor mass in the region of

either kidney. X-ray or radium therapy affords the only hope of relief as these cases cannot withstand the shock of an operation. At best the prognosis is poor.

The Gonadal Type.—Illustrative of this type is the well-known case reported by Sacchi. This boy at the age of nine years weighed ninety-seven pounds and had secondary sex hair, a deep voice, well developed genitalia with frequent erections and seminal emissions. After the removal of an alveolar carcinoma of the left testicle the voice became child-like, the erections and seminal emissions ceased and the secondary sex hair grew gradually less pronounced.

It is well known that the thymus shows signs of involution at the age of puberty and Marine and Manley have hastened sexual maturity in young animals by removal of the thymus, and Hewer has found that the feeding of thymus gland to young male white rats delayed testicular development. Clinically, thymus feeding has been found efficacious in delaying puberty in the human species but as yet there is not sufficient pathological evidence to justify the designation of a thymic type of precocious puberty.

Despite the foregoing data, it is not to be assumed that precocious puberty is only associated with tumor formation. These cases are quoted merely to show the interglandular relations. Many cases of precocious puberty live to a ripe old age and apparently even without therapy are none the worse for their early maturation. Stone reports a case of maturity at the age of four years, who, as far as is known, is still living and well. The father of this patient attained puberty at the age of eight (Lespinasse). The majority of these cases encountered develop between the ages of ten and twelve years. There is usually no gross pathological change demonstrable in any of the incretory glands; hence they cannot be grouped according to type. Treatment in these cases is instituted not alone to arrest the sexual precocity but likewise to obviate the associated symptoms which may exist, such as stunting of the growth, muscular asthenia and, most important of all, the behavioristic abnormalities so often exhibited by these patients. Many glandular combinations have been tried in this condition, but in the opinion of the writer a combination of thymus and pineal feeding has proved most satisfactory. Certainly it is the most rational. Dosage: thymus, desiccated gland, gr. 5, twice daily after meals; pineal, gr. ⅕, twice daily, after meals.

Hypersecretion in the Adult.—Excessive gonadal activity in the male after puberty is a condition frequently present but usually encountered by the physician only as a result of inadequate marital relations. The husband asks medical attention for his wife because of lack of desire and the wife in turn accuses the husband of satyriasis. As either, or both, may be right, and as the psychical element in such cases is fraught with such harmful possibilities, these patients require very careful consideration.

The diagnosis of excessive gonadal function rests mainly upon the frequency of erections and emissions. The affective element or libido is not dependable, as it is frequently of purely psychogenic origin and the sexual appetite so aroused far outmeasures the actual sexual power of the individual. As a general rule, the patient who demands intercourse more than twice a week, or has seminal emissions at more frequent intervals, may be held guilty of excessive gonadal function. Of course, the age and recentness of marriage are factors to be taken into consideration.

The causes of such hypergonadal activity are numerous. Good food, regular hours, plenty of sleep coupled with an active outdoor life and infrequency of sexual intercourse will produce a condition of increased sexual activity in every normal male. Soldiers, sailors, lumberjacks, prospectors and cowboys furnish examples of this class. Besides a paucity of sexual gratification there is a libidinous psychical trend nurtured by the lewd and obscene stories which form such a large part of the conversation of this class of men. This condition is by no means confined to the great outdoors, however, but is not uncommon in the large industrial centers as well. Here again we must distinguish between the psychical sexual appetite, often an aberrant psychosis, and real excess of sexual power. Lack of association with the opposite sex and lack of gratification do, however, favor excessive testicular activity as surely as the reverse is true.

Intrinsically, increased activity of the anterior lobe of the pituitary, of the suprarenal cortex and of the interstitial cells of the testes are likewise capable of causing this condition even in individuals not favored with such an invigorating form of life as those mentioned above. Increased sympathetic activity will produce the same condition.

Treatment.—Therapy in this condition includes psychotherapy, physiotherapy and medication. Psychoanalysis may be of value in some cases but usually rationalization and suggestion will suffice. Intensive occupation, exhaustive exercise and hot baths on retiring are excellent physical measures. It has been observed that glandular products are of little value in the treatment of this condition. The coal-tar derivatives, particularly acetanilid, the bromids and luminal are the most useful drugs in these cases. The dosage must be varied to meet the requirements of each individual patient.

Satyriasis.—Markedly increased libido without increased sexual power is not rare. It is occasionally found in cryptorchidism, at the male menopause, in X-ray and radium workers following impotence from exposure, and in the initial stages of organic testicular disease. Experimental work has shown an increase in the size and number of the interstitial cells in these conditions and it would seem likely that there is such a glandular basis for this disease. This state is most likely to develop in individuals of unstable nervous and mental equilibrium and an excessive

incretory action upon an unstable psyche or a libidinous trend overstimulating an otherwise normal interstitial secretion would undoubtedly produce the same end result.

The *treatment* is along the same lines as that outlined above.

Hyposecretion

Anatomical Anomalies—*Hermaphroditism and Pseudohermaphroditism.*—As far as known, true hermaphroditism has never been described in the human. Diagnosis of sex in the false types is possible usually only at autopsy or following biopsy as this rests upon the character of the sex glands, which are nearly always concealed, regardless of the type of external genitalia present. Treatment in these cases is along the same lines as that for cryptorchidism which will be taken up later. Treatment, however, is usually unsatisfactory.

Cryptorchidism.—This condition may result from any one of a number of anatomical variants, such as defects of the mesorchium, paralysis, absence, or faulty insertion of the gubernaculum, narrowness of the vaginal process, or large size of the testicle, shortness of the spermatic cord, rudimentary, or obliterated scrotum, premature obliteration of the inguinal canal, or from adhesions within the abdomen involving the inguinal canal following inflammation or trauma (Davis).

Migration of the testes may be arrested within the abdominal cavity, at the internal ring, or within the canal (inguinal extopia—the common variety). Migration may be aberrant and the testicle may take one of the following abnormal positions: in the small pelvis; the deep crural; superficial crural; cruroscrotal; pubopenile; penile; subcutaneous abdominal, or perineal (Davis). Further, a patent vaginal process may permit an intermittent migration of the testes.

One or both of the testicles may be involved in this process. The most common form is unilateral cryptorchidism. This is a common complaint in children, but nearly all of these cases clear up with the advent of puberty or shortly afterward. Descent may occur as late as the fifty-eighth year (Sebileau and Descomps). Unless the pathological anatomy absolutely prevents the descent of the testicles, this process may often be hastened by feeding pituitary and thyroid substance in doses up to the limit of tolerance over a period of several months. Results are often obtained within as short a period as one to two weeks. The production of bitemporal headaches is the sign of overdosage of pituitary, and occipital headaches, palpitation and increased irritability are indicative of too much thyroid.

Before puberty these cases show, besides undescended testicles, small genitalia and a tendency to a scrotal fold encircling the base of the penis.

At the usual age of puberty they fail to mature and usually grow very rapidly in height. The beard and secondary hair is slow in appearing and when it does put in appearance it is sparse and usually reversive in type. Their adult characteristics are those of the eunuchoid and will be discussed later.

Aspermatogenesis is the rule in these cases, exceptions are rare. Likewise, libido is usually lacking or diminished, though it may be present or even increased for a time as explained above.

Treatment.—Treatment should be started early and it is to prevent if possible the later development of a eunuchoid state that I advocate the treatment of all cases of cryptorchidism after the age of five years. Treatment should be persisted in even in the later cases as benefit is occasionally given even at the age of thirty or forty years. The percentage of failure in these later cases is much higher than that of the successes and the prognosis should not be painted to the patient in too rosy terms. As indicated above, the treatment consists in feeding thyroid and pituitary substance to the limit of physiological tolerance. This treatment may be supplemented by small doses of sodium iodid, gr. 5, every day or every other day. A very satisfactory method of administering pituitary in these cases is anterior lobe pituitary, 1 gr.; whole gland pituitary, ½ gr., placed in capsules and administered about halfway between meals, once, twice or three times daily, as the case may require. The reason for giving pituitary midway between meals is because it sometimes causes unpleasant gastro-intestinal symptoms such as colicky pains, nausea, etc., if administered shortly before or directly after a meal. In refractory cases, injections of anterior lobe pituitary, 1 c.c. hypodermically, once a week, may prove of value. The feeding of suprarenal cortex in these cases has been disappointing but it is worth while trying when other measures fail. This product is prepared in powder and tablet form; the average dosage is 2 gr., twice daily, after meals.

Degenerative Changes.—The cryptorchid states have already been considered.

Hypopituitarism.—Fröhlich and later Cushing and Goetsch have established this syndrome. Insufficiency of the anterior lobe of the pituitary for any reason produces hypo-activity of the gonads. Fröhlich's dystrophoadiposogenitalis is a good example. The girdle distribution of fat about the hips, the fat pads about the breasts and above the knees and elbows, the increase of breadth of stature at the expense of height, the small genitalia and tapering fingers serve to make the diagnosis. X-ray of the skull invariably reveals a small inadequate sella turcica. While the hereditary factor is the usual etiology in these cases, this condition may also be acquired from disease of the pituitary. Such a hypopituitary state is quite frequent following encephalitis. The administration of pituitary substance as outlined above is very satisfactory in these cases.

Persistent Thymus.—This type evolves into the thymus-suprarenal-pituitary compensatory syndome (Timme) which has already been described.

Hypothyroidism.—The cretinoid states also show hypogenitalism. This condition clears up on thyroid feeding.

Senility.—"In old age, the testes may become smaller, softer and browner, or harder and more fibrous. The first form is considered normal and in it, while the tubules are narrowed and somewhat thickened, spermatogenesis persists. In the second form, there is an overgrowth of fibrous tissue, the epithelial elements disappear, the Sertoli cells persisting longest, and spermatogenesis ceases. Normally, potency should last until the seventieth or eightieth year, sometimes longer. The interstitial cells survive the spermatogenic elements, and therefore libido often outlasts fecundity. In old testicles small scars are often seen, due to obliteration of some of the tubules, and are said to occur more frequently in arteriosclerotics" (Davis). Accompanying these changes there often occur additional symptoms comparable to those of the female menopause, namely, increased irritability, anxiety, depression, emotional instability, palpitation, flushings, paresthesias and not infrequently increased libido. It is for these latter symptoms that treatment is usually instituted.

Treatment.—Orchitic substance, gr. 2, twice daily, after meals, together with hypodermic injections of cacodylate of soda, gr. ¾, three times a week, will often control the situation. If this treatment proves inadequate it may be supplemented with small doses of luminal.

Toxic Conditions.—Any poison capable of causing degenerative changes elsewhere in the body may likewise produce degenerative changes in the testes. Alcohol is credited with a selective action on the spermatogenic cells, leaving the interstitial elements unharmed, thus destroying fecundity and preserving the libido. Extensive destruction of the liver is accompanied by testicular degeneration.

Irradiation.—As has been noted above, exposure to X-ray or radium produces atrophy of the seminiferous tubules without harmful action on the interstitial cells. Prolonged exposure will produce complete atrophy of all the testicular elements.

Traumatism.—Degenerative changes may be produced by contusions and wounds injuring the testes directly or by damaging the blood supply or vas deferens.

Inflammation.—Degeneration may follow inflammation of the testes or of the testicular appendages, namely, the epididymis, vas deferens, or seminal vesicles. The inflammation may be acute or chronic. Infection, the chief causative agent of inflammation, may take place either by way of the efferent duct or through the blood-stream. Gonorrhea most frequently finds its way to the testes via the efferent ducts, but all the pus-forming organisms have at times used this avenue of entrance. Among

the hematogenous infections causing acute inflammation are variola, typhoid fever, scarlatina, influenza, pneumonia, rheumatic fever, pyemia, meningitis, Malta fever, vaccinia and pyocyaneus. Chronic inflammation may be due to tuberculosis, syphilis, the mycoses, glanders, leprosy, filariasis, malaria, or echinococcus.

Tumors.—Any metastatic tumor may involve the testes secondarily. Primary tumors arising from all the various parts of the testis and its adnexa have been described. These include fibroma, sarcoma, carcinoma, adenoma, lymphosarcoma and teratoma.

Treatment.—Treatment of the above conditions is primarily that of the causative agent. Unless complete atrophy has taken place, hope of return of function should not be despaired of, especially if the subject is young. Loss of spermatogenesis is less likely to be restored than function of the interstitial cells. Treatment as outlined above for cryptorchidism is helpful in these cases. Chevassu reports a case in which healthy spermatozoa were recovered from a testicle which had been obstructed by an old gonorrheal process for thirteen years.

Impotence.—This condition is one in which fecundity is destroyed without change in the secondary sex characteristics. Libido, while usually modified, is still present. Erections are frequent and flabby. Impotence is an adult disease, developing in a previously normally functioning male as a result of any of the above-mentioned causes in which the process of degeneration has involved only the spermatogenic elements and has not attacked the interstitial cells. Gonorrhea far outnumbers all others as a causative factor in this particular condition. Sexual excess will produce at times a somewhat similar picture, though, precisely speaking, this is really a transient eunuchoid state as both testicular functions are involved.

Treatment.—Orchitic substance has proved of little value in this condition. Treatment is directed mainly toward the restoration of a normal erection and orgasm in which case, if any normal spermatogenic elements remain, fecundity will also return. Pituitary desiccated gland, gr. 2, particularly the anterior lobe, and the sympathetic stimulants, such as thyroid, suprarenal gland and strychnin, are most useful. The dosage must be regulated to the tolerance of each individual.

The Eunuch.—This type of individual is the result of complete absence of testicular activity and is usually an acquired state, as congenital absence or atrophy of both testicles is an extremely rare condition. Either accidentally or by design, surgery is responsible for the production of the great majority of these cases. Inflammatory degeneration is a factor of secondary importance as an etiological factor. Excessive sexual function is capable of causing this condition as is admirably illustrated by the method of producing eunuchs among the descendants of the old Aztec tribe of Mexico. The religious ceremonies of this tribe call for the

presence of a certain number of individuals called Mujerados. These men are eunuchs and they are produced by the following unique method.

"The man, anywhere from twenty to thirty-five years of age, is masturbated several times daily, and made to ride horseback constantly. This treatment soon produces an irritable weakness, so that the act of horseback riding produces ejaculation. Gradually as this régime is continued, the testicles atrophy, the penis atrophies, and the pubic hair may or may not disappear. In addition to this, these men's breasts are suckled by babies, and consequently they develop markedly. The bodily shape is not markedly feminine but remains more or less masculine. The scrotum is shrunken and the testicles are very small and not particularly sensitive to pressure" (Lespinasse).

Description.—If castration takes place before puberty, as it frequently does, there is a characteristic skeletal change. Union of the epiphyses is delayed. The bones of the extremities remain slender but increase in length with the end result that the arms and legs are much too long for the trunk. The pelvis approaches the female type. These patients are loose-jointed, awkward, and have a tendency to genu valgum. The larynx remains small and the voice high-pitched and childlike: In castration after epiphyseal union has been effected, no skeletal change takes place. In castrates after puberty, the voice often becomes higher and assumes a shriller quality. The skin is pale and soft; that of the face assumes a yellowish, parchmentlike appearance with a tendency to wrinkle, thus giving the old and worried look so characteristic of the eunuch. Secondary sex hair assumes an undifferentiated character. It is sparse and fine on the face and chin. Axillary hair is scant and pubic hair is limited to the mons and shows the feminine, horizontal demarcation. Deposits of fat about the hips and breasts lend a feminine contour to the figure. The penis is small and erections and ejaculations usually are absent. If present, the erection is of short duration and the ejaculation thin and watery.

Temperamentally, the eunuch is rather quiet and phlegmatic. He lacks aggressiveness and shows a general reversion to the puerile attitude. The eunuchs of Constantinople are avaricious, illogical, obstinate, possess little judgment and accept information without proof. As a rule, they are fond of children and animals and are faithful in their affections, but possess little courage. Their mentality is often deficient and they are very fanatical. Eunuchs of high intellectual ability, however, are not uncommon (Hikmet and Regnault).

Treatment.—As above stated, the feeding of orchitic substance is inadequate in the treatment of hypotesticular function and so it proves in the case of the eunuch. The pharmacodynamics of the testes as yet remain undeterminate. No pure extracts of the interstitial cells have been obtained and no active principle of the testes has yet been isolated. The

feeding of orchitic substance, as it is now available upon the market, is not without benefit in supplementing a mildly decreased testicular function, but it is wholly inadequate to supplant a marked or total loss of function.

Tandler reports a case of one of the Skoptzi who had been castrated at the age of twenty-one, but who continued to practice coitus daily. The erection was of short duration, the orgasm hurried and the ejaculation thin and watery, nevertheless, it was sufficient to permit intercourse. In all other respects, this man was a typical eunuch and Tandler assumes that compensatory activity of the pituitary and adrenal cortex accounted for the persistance of the libido in this instance. This assumption is more or less borne out by clinical evidence. Under pituitary and adrenal cortex feeding, such as has been previously described, there will be improvement in the mental sphere and the patient will tend to approach the various obstacles of his daily existence in a more adult fashion; further, the libido may in part be restored. Little change is usually effected in the other eunuchoid characteristics.

Lespinasse is heartily in favor of human testicular transplants in these cases. He reports a case in which a man of thirty-eight, who had lost one testicle through a herniotomy and the other through an injury, consulted him because of inability to have intercourse. A testicle was transplanted into the rectus abdominalis muscle and four days after the operation the patient experienced a strong erection and marked sexual desire. Libido remained well marked in this patient for five years, after which time he was lost track of by Lespinasse. Two of my own patients have had the benefit of testicular transplants; both of these cases showed marked improvement for approximately six months, after which they relapsed into their former state. Subsequent exploration in one of these cases revealed a complete fibrous atrophy of the transplant.

The acquisition of suitable material for transplantation is a problem, in spite of the fact that Lespinasse expresses himself as surprised at the number of testicles available for this purpose. Granting that a suitable and willing donor may be obtained, which in my experience has been very difficult, extremely unpleasant complications of law and ethics may arise later, especially at the present time when news of this sort is so avidly exploited by the press. Nevertheless, if circumstances are reasonably favorable, this is a therapeutic measure well worth trying. As far as my own experience is concerned, heterogeneous transplants have not proved of value.

Eunuchoidismus.—Eunuchoidismus is the adult form of hypogonadal activity in which the functional elements of the testes are partially but not totally destroyed. The child who manifests lack of testicular activity, either congenital or acquired, will show the eunuchoid state after puberty; likewise, the normal adult suffering partial degeneration of the testes

from any of the causes already mentioned, in which both the spermatogenic and interstitial elements are involved, will come within this classification.

The clinical manifestations of this condition vary from the almost normal individual to the type in which gonadal activity is so diminished as to be almost indistinguishable from the true eunuch. The signs and symptoms of this condition are of the eunuch type and differ therefrom only in degree or intensity. Many mild types of eunuchoidismus go through life perfectly compensated as a result of increased activity of the pituitary and suprarenal cortex; others decompensate upon occasion of great physical or mental stress and still others fail to compensate fully at any time. These variants tend to confuse the clinical picture of this disease entity, but if the fundamental relations of the sex glands to the pituitary and adrenal cortex are borne in mind, such confusion may be obviated.

Treatment.—The treatment outlined for the eunuch is not only applicable to the eunuchoid states but usually more efficacious. The feeding of orchitic substance is of much value in the milder forms. The optimum dosage in the average case is orchitic substance, desiccated gland, gr. 2, twice daily, four days out of seven.

In addition to the therapeutic measures outlined under the therapy of the eunuch, there is yet another measure which deserves mention here and that is the Steinach operation. This operation was designed particularly to combat the lack of interstitial secretion in senescence, but it is likewise applicable to any of the eunuchoid states. The procedure is simple and consists merely in the ligation of one or both of the vas deferens. The rationale of this operation was established by Steinach through experimental work on animals, principally the white rat, in which he showed that ligation of the vas deferens produced degeneration of the spermatogenic elements and hypertrophy of the interstitial cells, together with changes in growth and behavior indicative of an increased gonadal activity. This experimental work has been confirmed by Knud Sand. In his original paper in 1920, advocating the use of this operation for rejuvenating the aged, Steinach cites two cases which showed marked improvement following unilateral ligation of the vas. One was a case of premature senility, aged forty-four, with loss of weight, flabby muscles, depression, asthenia and tremor. Following the operation, the patient showed full return to vigor, alertness and capacity for hard work. The other patient suffered the effects of senility at the age of seventy, was rejuvenated by unilateral ligation of the vas deferens and was still feeling well and strong two years after the operation.

No comprehensive reports of the use of this method are yet available. Isolated instances of the employment of this operation are encountered now and then, and some physicians in this country are employing this procedure quite extensively, but they have not as yet seen fit to publish

their results. I have never recommended this procedure to any of my patients and the patients upon whom I have seen it used have been little benefited. I freely admit that my experience is insufficient to permit a logical conception of the value of this method, so judgment is withheld until further evidence is accumulated. The striking results produced experimentally in lower animals would seem to foreshadow a definite usefulness in the human species; this, however, has yet to be demonstrated.

DISEASES OF THE FEMALE GONADS

Functions.—Aside from the function of ovulation the ovaries exercise a determinate action on the formation of secondary sex characteristics in the female. Extirpation of the ovaries in the human before puberty develops an undifferentiated adult possessing many of the attributes of the eunuch (Marshall). Extirpation of the ovaries after puberty results in the reversion of the female to the undifferentiated type without the skeletal change of the earlier castrate. Steinach's classical work on the transplantation of ovaries in castrated animals is very convincing evidence of the effect of the ovarian secretion on the development of the secondary female sex characteristics. From the fact that the true luteal structures in these transplanted ovaries degenerate leaving a preponderance of inner thecal cells and interstitial cells, it is postulated that the development of the female secondary sex characteristics is dependent upon an internal secretion elaborated by these latter cells. This view is corroborated by X-ray experiments in which ovulation is inhibited by exposure to the Roentgen ray. Microscopical examination of ovaries so treated reveals no normal follicles or corpora lutea yet the secondary sex characteristics remain unchanged.

The Rôle of the Ovary in Menstruation—*Modern Conception of Menstruation.*—It has been known for more than a hundred years that the occurrence of menstruation is dependent upon the ovaries. Until comparatively recent years it was believed that the ovarian influence is exerted through the medium of the nervous system. This indeed was the basis of the theory of Pflüger, enunciated in 1865, and quite generally accepted for many years. According to this theory, menstruation was to be looked upon as due to a reflex pelvic hyperemia, evoked by afferent impulses originating in the terminations of the ovarian nerves, as a result of the pressure of the growing graafian follicle. This theory was convincingly disproved by the work of Knauer, Marshall and others, who showed that menstruation, or the corresponding phenomena in lower animals, still continues after the removal of both ovaries, provided they were transplanted into some other part of the body. In other words, the ovarian influence is blood-borne, that is, it is of the hormone nature.

Which Constituent of the Ovary is Concerned with Menstruation?—As to which constituent of the ovary is responsible for the internal secretion so essential for the occurrence of menstruation, we cannot as yet speak with precision. The weight of evidence is overwhelmingly in favor of the view that it is the corpus luteum which has this essential rôle. Some authors, like Marshall and Runciman, are inclined to the view that it is growing graafian follicles which are most concerned. Still others attach much importance to the so-called interstitial cells, although these cells in the human female are well developed only in the pregnant state. For a full discussion, the reader is referred to the numerous special articles dealing with it.

Mechanism of Menstruation.—To summarize the prevailing views, it may be stated that the corpus luteum, beginning its life history at the time of ovulation, passes through a series of developmental stages which reach the acme just before the onset of the next menstrual period. Hand in hand with this development of the corpus luteum there proceeds a similar hypertrophic change in the endometrium, also reaching its high point (premenstrual stage) just before the onset of the next period. The clinical phenomenon of menstruation, with its discharge of blood, is indicative of a catabolic or destructive process in the endometrium when conception does not occur. It is a transition of the endometrium from the highest to the lowest point of its development. On the other hand, if the ovum has been impregnated, the premenstrual hypertrophy of the endometrium passes on by easy stages into formation of the early decidua.

So much seems to be well supported by the evidence at hand. It should perhaps be emphasized that while the corpus luteum is essential for menstruation, it is not, of course, the cause of the actual menstrual hemorrhage. The rôle of the corpus luteum is to prepare the endometrium for the reception of a possible impregnated ovum. The actual menstrual discharge is synchronous with the beginning of retrogression in the corpus luteum, as Labhardt emphasizes in his recent article. The influence responsible for this has not yet been determined, but there is reason to believe that it is associated in some way with the ovum discharged at the previous ovulation. Perhaps it is the death of this ovum which determines the beginning of the retrogressive changes in the corpus luteum and in the endometrium (Emil Novak).

Hypersecretion

Precocious Puberty.—Precocity in the female is not unlike, in its causes and development, that which I have already described for the male sex. It is characterized by the appearance of sex consciousness, the onset of menstruation, the enlargement of the breasts, the rounding out of the hips and thighs, and the development of pubic and axillary hair. It is

interesting to note that no cases of sexual precocity associated with pineal tumor have ever been reported in the female, although often pineal shadows are seen on X-ray examination. No cases of precocious puberty associated with pituitary tumors have been reported in either sex. Beekman reports the case of a girl of six and one-half years with large firm breasts, well developed axillary and pubic hair, an adult type of vulva and irregular menstruation. X-ray of the skull revealed an enlarged and eroded sella turcica. The treatment and prognosis in these cases is the same as that detailed under this heading in the section on the male gonads. It is to be remembered that these cases are prone to sexual violations and this danger should be carefully guarded against.

Hypersecretion in the Adult.—Hypergonadal secretion in the adult female is a baffling and difficult subject. It is impossible to separate the libido from sexual power as we endeavored to do in the male. Exceptional fecundity, as evidenced by numerous pregnancies, fifteen to twenty, and prolongation of the childbearing period, that is, postponement of the menopause until well along in the fifties or later, are evidences of increased ovarian activity. Usually the libido is not increased in these cases, nor are these conditions so undesirable as to necessitate treatment. Increase of libido unless it is marked is very difficult to diagnose. Marked increase of libido, nymphomania, exists most frequently in socially maladjusted individuals and as such requires reëducation and specialized psychotherapy. In all these cases a possible source of local irritation should be carefully sought for and if possible eliminated. Likewise if any endocrinopathy is noted the case should be treated along these lines. The causes of this condition are too various to admit of any definite rules of treatment.

Hyposecretion

Hypogonadal activity may be due to anatomical anomalies ranging from almost complete agenitalism and pseudohermaphroditism to the slightly undersized uterus so often found in dysmenorrhea, or to degenerative changes resulting from disturbances of the pituitary, thyroid, thymus, or suprarenals; senility; intoxications; irradiation; traumatism (including both surgical and accidental); tumors, or infections. The symptoms vary with the age of onset and the severity of the process.

Complete loss of ovarian function before puberty results in a female eunuch state. Menstruation is never established. The breasts remain undeveloped. There is a tendency to reversive hair distribution. The arms and legs are too long for the body. The buttocks are lean and sexual feeling does not develop. Treatment is of little or no avail in these cases.

The Menopause.—This condition has been described as the withdrawal of the internal secretory activity of the ovaries. Sanes reports the average age at which this phenomenon normally occurs as forty-seven

and one-tenth years. Due to any of the above-mentioned causes the menopause may occur at any time after the establishment of puberty. Regardless of the age of appearance the following symptoms are observed:

1. *Cessation of Menstruation.*

2. *Vasomotor Symptoms.*—These include hot flushes, chilly sensations, sweating, vertigo, faintness, vicarious bleeding (may occur from any mucous surface, most commonly from the nose), tachycardia, numbness and tingling of the hands and feet and various paresthesias. Novak states that vasomotor symptoms are met with in varying degree in 80 per cent of all cases.

3. *Nervous Symptoms.*—These symptoms are not always present but are not uncommon. They include excitability, irritability, increased fatigability, emotional instability and a tendency to worry over little things.

4. *Psychic Disturbances.*—These disturbances vary from mild depression and phobias to actively hallucinated states. The milder forms are not uncommon. Fortunately the severer forms are rather rare.

5. *Anatomical Changes.*—Besides the degeneration or destruction of ovarian tissue, there is atrophy of the subcutaneous tissue of the external genitalia with resultant shrinkage, the glandular elements of the generative tract undergo degenerative change and the uterus becomes small and fibrous. The glandular substance of the breasts disappears and in a large proportion of women there is an increase in body weight.

6. *Diminution or Loss of Sexual Desire.*—Frequently in the normally occurring menopause the sexual appetite is preserved and even at times increased after the cessation of menstruation. This may be explained by the fact, which has been confined by histological studies, that the germinal epithelium disappears before the interstitial elements in senile degeneration of the ovary and occasionally the interstitial cells exhibit a transient hypertrophy at this time. At any rate the sexual feeling gradually disappears, as eventually all the ovarian elements are replaced by fibrous tissue.

Treatment.—Treatment is directed mainly toward the amelioration of the vasomotor, nervous and psychic symptoms described above. The cessation of menstruation, anatomical changes and loss of sex feeling must at the present state of our knowledge be borne with philosophy as a necessary accompaniment of increasing years, despite the much-heralded practice of ovarian transplantation. Opotherapy has proved of great benefit in controlling the unpleasant vasomotor, nervous and milder psychic symptoms which accompany menopause. The real involution psychoses require psychiatric care in addition to organotherapy.

Ovarian extracts are, on the whole, the most useful and beneficial. Although some writers report striking results with the whole gland substance, my own best results have been obtained with corpus luteum extracts

in the earliest phases of the condition, and this in relatively small doses, gr. 1 to 2, twice daily, four days out of seven. This may be supplemented by injections of the liquid extract, which is conveniently put up in ampule form, either subcutaneously or intravenously, two or three times a week. Improvement will be noted usually within the first week of treatment. In cases in which fatigability is a prominent symptom, small doses of suprarenal gland, gr. ½, twice daily, with or without corpus luteum, is of great value. Frequently hypothyroidal symptoms are evident, such as brittleness of the hair and nails, puffiness of the face, thinning out of the hair, etc. In these cases thyroid should be fed to the limit of tolerance. Small doses of sodium iodid, gr. 2 to 5, once daily are also helpful. I employ small doses of pituitary substance, gr. ¼ to ½, once daily, in all menopausal cases, as I find that the result is much better than from corpus luteum alone. Experimentally, there is a very close relation between the pituitary and ovary and this is emphasized by clinical experience. In the latter phases, during which we frequently find high blood-pressure, ovarian substance without luteum in 5-gr. doses, two or three times daily, is advisable.

While Steinach has developed the technic of ovarian transplantation to a high degree in white rats, the advantages of this procedure have yet to be demonstrated in greater numbers than at present in the human species. Bordier reports rejuvenation in the female at the menopause following irradiation of the ovaries, explaining his results by a transient hypertrophy of the interstitial cells following destruction of the germinal elements which are more susceptible to the X-ray. Bordier's results have not been confirmed by other investigators.

Amenorrhea and Oligomenorrhea Due to Hypogenitalism.—Intelligent treatment of these conditions hinges upon an intelligent concept of the cause. It may be well to recapitulate to some extent and consider the causes of hypogonadal activity, of which amenorrhea and oligomenorrhea are symptoms. Besides those causes already enumerated, we must bear in mind that varying periods of amenorrhea are encountered at puberty and near the menopause, referred to by Novak as physiological amenorrhea. Amenorrhea is the normal status during pregnancy and is the rule during at least the first part of the period of lactation. Failure of menstruation may be due to psychic causes such as fright, fear of illicit pregnancy in unmarried women and that interesting phenomenon described as "pseudocyesis." Change of climate and environment is at times a cause of transient amenorrhea. Novak makes the following pertinent statement:

"In a much larger proportion of cases than is commonly believed, amenorrhea or oligomenorrhea are the results of endocrine disorders rather than a pelvic disease. This is in contrast with the etiology of ex-

cessive menstruation, which is to be sought in local pelvic disease far more frequently than in constitutional causes, endocrine or otherwise."

Treatment.—Therapy, necessarily, is first directed at the cause. Drugs are of little value except in the treatment of an underlying systemic disease such as chlorosis. Our chief weapon in this condition lies in endocrine therapy. Whole gland ovarian extract should be administered either by mouth or by hypodermic injection, preferably by mouth, as it is often necessary to continue the medication over a considerable period of time. The dosage is gr. 2 to 5, twice daily after meals. This should be accompanied by pituitary therapy. A good average combination to start with is anterior lobe pituitary, gr. 1, whole gland pituitary, gr. ½, desiccated gland, placed in a capsule and given once daily, halfway between meals. This dose should be gradually increased to anterior lobe pituitary, gr. 2; whole gland pituitary, gr. 1, three times a day, if it is possible to do so without producing headaches. The influence of suprarenal cortex is strikingly emphasized in cases of precocious puberty associated with hypernephroma, and its administration is undoubtedly justified in cases of hypogonadal activity. Clinically, the results are not as brilliant as are obtained with ovarian and pituitary feeding, but nevertheless it is worth trying in refractory cases. Suprarenal cortex may be prescribed in powder or tablet form. The dosage is gr. 2, by mouth, twice daily, after meals.

The opotherapy outlined above is of use in all forms of amenorrhea or oligomenorrhea regardless of cause. Needless to say this form of therapy should not be employed if the patient is acutely ill. The causative factor deserves first consideration and should be carefully sought for and if possible eliminated. If the basic trouble appears to be an endocrine disorder, as frequently happens, the results are more satisfactory. The particular type of disturbance should be determined and emphasis laid upon correcting the gland at fault.

Primary Dysmenorrhea.—By this is meant that form of menstrual pain not associated with any demonstrable form of pelvic disease. Novak gives the following causes: (1) Mechanical obstruction of the cervical canal; (2) the neurotic factor; (3) hypoplasia of the uterus. The last two causes undoubtedly have an underlying endocrine factor in a large percentage of cases. Primary dysmenorrhea is essentially a gynecological condition. If gynecological measures fail to bring relief organotherapy may be resorted to.

Glandular Therapy.—The typical neurotic type will often give somewhat the following history: The periods usually occur early, that is, every twenty-one to twenty-six days. For a week to ten days before the onset, the patient is nervous, excitable, depressed, apprehensive and gives way to tears on the slightest provocation. Often they exhibit tachycardia, and slight enlargement of the thyroid gland. Fatigue is a common symptom.

The onset of menstruation is characterized by great weakness, sometimes nausea and vomiting, severe cramplike abdominal pains, backaches, and cramps in the muscles of the legs. The patient is usually confined to bed for the first day or two of the period, and sedatives are often necessary to control the pains. Careful examination will often reveal signs of underfunction of the thyroid, suprarenals, or pituitary or any combination of these. Furthermore, the early or rather frequent menstruation indicates an inadequate corpus luteum secretion.

These patients often do well on the following régime: Beginning a week or ten days before menstruation is due, depending upon the time of onset of the nervous symptoms, corpus luteum should be given to these patients, usually gr. 2 by mouth, twice daily. This should be continued until the first day of menstruation. During the remainder of the month the underlying glandular deficiency should be treated by administration of small doses of thyroid, suprarenal or pituitary as the case may be.

Those types of dysmenorrhea associated with hypoplasia of the uterus are not so satisfactory to treat. Occasional good results are obtained by glandular therapy, especially in young subjects. Treatment is directed towards promoting the growth of the uterus. Ovarian and pituitary therapy is used similar to that laid down for amenorrhea and oligomenorrhea in the preceding paragraph. In addition subcutaneous injections of the liquid extract of the anterior lobe of the pituitary, in doses of ½ to 1 c.c., should be given two or three times a week.

Functional Uterine Bleeding.—There is a type of uterine bleeding in which no local pelvic disease can be demonstrated. This type is variably referred to as idiopathic, essential or functional uterine bleeding and may reveal itself either as a metrorrhagia or menorrhagia, usually the latter, and is more frequently evidenced at the time of puberty or near the menopause. The nature of this disturbance and the time of occurrence would seem to indicate some type of endocrine disturbance, the nature of which is not yet clear. Novak believes that it is due to a disturbed ovarian function and advances considerable evidence to support this view.

Treatment.—It must be borne in mind that we are speaking now of uterine bleeding for which gynecological procedures have failed to reveal the cause and have failed to benefit. Opotherapy more or less empirically used has at times proved of benefit. Broadly speaking thyroid therapy is most satisfactory in this type of bleeding occurring at the age of puberty, while corpus luteum therapy proves most beneficial in this condition when associated with the menopause. Numerous exceptions to this rule will be found, however. Pituitary therapy, especially injections of pituitrin, at times proves of value. Unfortunately, the treatment of this condition is still a trial and error process and no definite rules of treatment can be laid down.

A general statement may here be added in the treatment of the fore-

going conditions with lutein. It is not a good plan to give lutein regularly without intermission. Usually, to conform more or less to the natural processes, it ought to be omitted for one week in every four, the week during which normally no lutein secretion is produced in the body. Furthermore, I have seen a number of cases resembling anaphylactic shock, acidosis and allied states produced apparently from a too long continued use of lutein.

REFERENCES

Beekman, F. Arch. Pediat., xxxii, 4-19, 1915.
Bordier, H. Monde méd., No. 573, July, 1920.
Bouin, P., and Ancel, P. Compt. rend. Soc. de biol., Paris, lv, 1682-1684, 1903.
Chapin, C. L. Journ. Exper. Zoöl., xxiii, 453-482, 1917.
Cowdry, E. V. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Cushing, H. The Pituitary Body and Its Disorders, Clinical States Produced by Disorders of the Hypophysis Cerebri, Philadelphia and London, J. B. Lippincott & Co., 1912.
Davis, D. M. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Felix, W., Keibel, F., and Mall, F. P. Manual of Human Embryology, Philadelphia and London, J. B. Lippincott & Co., 1912.
Fröhlich, A. Wien. klin. Rundschau, xv, 883-906, 1901.
Goetsch, E. Johns Hopkins Hosp. Bull., xxvii, 29-50, 1916.
——— Surg., Gynec. & Obst., xxv, 229-243, 1917.
Hansemann, von, D. Arch. f. path. Anat., etc., cxlii, 538-546, 1895.
Hewer, E. E. Journ. Physiol., l, 434-437, 1916.
Hoskins, R. G., and Hoskins, A. D. Arch. Int. Med., xvii, 584-589, 1916.
Jump, H. D. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Lecaillon, A. Compt. rend. Soc. de biol., Paris, lxvi, 599-601, 1909.
Lespinasse, V. D. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Marine, D., and Manley, O. T. Journ. Lab. & Clin. Med., iii, 48, 1917-1918.
Marshall, F. H. A. Internat. Clin., Series 17, ii, 190, 1907.
——— Journ. Physiol., xliii, 247-260, 1911-1912.
Novak, E. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Rasmussen, A. T. Am. Journ. Anat., xxii, 475-515, 1917.
——— Endocrinology, ii, 363-404, 1918.

Regaud, C., and Dubreuil, G. Compt. rend. Soc. de biol., Paris, lxv, 393-395, 1908.
Sacchi, E. Riv. sper. di freniat., Reggio-Emilia, xxi, 149-161, 1895.
Sand, K. Journ. Physiol., liii, 257-263, 1919.
Sanes, K. T. Am. Journ. Obst., lxxiii, 93-212, 1916.
Sebileau, P. P., and Descomps, P. Maladies des organes genitaux de l'homme, Paris, J. B. Bailliere et fils, 1916.
Steinach, E. Arch. f. Entwcklngsmechn. d. Organ., xlvi, 557-619, 1920.
Tandler, J. Wien. klin. Wchnschr., xxiii, 459-467, 1910.
Timme, W. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Watson, A. Journ. Physiol., liii, 86-91, 1919.
Wheelon, H. Endocrinology and Metabolism, New York and London, D. Appleton & Co., 1922.
Whitehead, R. H. Am. Journ. Anat., iii, 167-182, 1904.

CHAPTER XVII

MULTIGLANDULAR SYNDROMES

WALTER TIMME

Introduction.—While this title at first glance would seem to be all inclusive, through usage in endocrine literature it has come to be limited to a few fairly definite clinical entities. Precisely speaking, at the present state of our knowledge there is no pure monoglandular disturbance without some concomitant disorganization of function of one or more of the other incretory glands. Further, the few syndromes which I shall hereinafter take up are not all-inclusive; as there undoubtedly are, as we shall perhaps learn in later years, other multiglandular syndromes upon whose existence we can only speculate and upon whose therapy we are committed to a state of empiricism.

I have used the following classification of multiglandular syndromes as a working basis.

1. Uniglandular syndrome with secondary or subsidiary pluriglandular manifestations.
2. Transitional groups.
3. Pluriglandular insufficiency syndromes.
4. Pluriglandular hyperfunctioning syndromes.
5. Pluriglandular compensatory syndromes.
6. Pluriglandular antagonistic syndromes.
7. Syndromes frustes.

Group 1 includes such disturbances as myxedema and Addison's disease in which the clinical and pathological picture is dominated by the disease of one particular gland and the concomitant disturbance of other glands is apparently insignificant. The description and therapy of these conditions have been taken up in another chapter.

Group 2 includes such types as Fröhlich's dystrophy which, to continue our illustration, is dominated by one gland, in this case a hypofunction of the pituitary; but the clinical picture is clouded by a rather profound disturbance of function of the thymus, thyroid and gonads as well. Like the first group, these types have been considered elsewhere.

Group 3 I shall take up in detail.

PLURIGLANDULAR INSUFFICIENCY

Description.—Perhaps the most widely recognized of the pluriglandular insufficiencies is that known and described by Claude and Gougerot as *insuffisance pluriglandulaire*. These writers describe a condition in which more or less simultaneously various glands of internal secretion gradually undergo atrophy and the manifestations of their insufficiencies become part of a clinical picture. This clinical picture is subject to the greatest variations, depending upon such factors as the intensity of the process on the several glands, the degree of the compensatory possibilities and the natural resistance of the patient. So that in combination with gonadal disturbances we may get Addison's suprarenal disease, or myxedema or a combination of acromegalia with exophthalmic goiter; in short, practically any combination of a deficiency character.

Etiology.—By far the greatest factor in the etiology is the hereditary one, predisposing the individual to the development of the syndrome as a result of various existing final causes. For a more complete exposition of this factor the reader is referred to my paper on endocrinopathic inheritance (Timme). The basic constitutional predisposition can occasionally be recognized even before the actual process has set in. The suspected individuals usually show in adolescence a delayed development of their gonadal activity. Women menstruate late; males have a delayed puberty with little sexual appetite. Both sexes are disposed to be asthenic. The final factor that ushers in the atrophic process may be of quite moderate significance for normal individuals, such as malaria, excessive use of tobacco (Hertoghe) or pregnancy; but usually the final cause is of rather severe nature, namely, the acute infections, influenza, scarlet fever, measles, diphtheria, acute articular rheumatism; or the metallic poisons, lead, arsenic and mercury. Alcoholic and drug habitués are prone to be affected. Occasionally, the syndrome is engrafted upon a previously existing cirrhosis of the liver. Possibly the most frequent causes are syphilis and tuberculosis (Poncet and Leriche; Faneau de la Cour). Agnosti cites chronic malaria, leprosy and pellagra as causative factors. In spite of this comparatively long list of exciting causes, it is in only a surprisingly small number of individuals that the sequel of pluriglandular insufficiency develops. The probability is that these diseases are not specific in their selection as far as the glands of internal secretion are concerned, but act simply as final critical determinants upon a system already weak or in an unstable equilibrium through inheritance or through a lack of compensatory possibilities. Traumatism may also play either a primary or secondary rôle in the production of the syndrome: primary, if through the trauma one of the endocrine glands is directly injured to such an extent that it cannot meet its physiological requirements, as in traumata of the supra-

renals or testicles; secondary, if general bodily injuries are of such extent and productive of such shock as to require more of the protective and stimulative secretions than can readily be supplied without producing exhaustion of the glands beyond the possibility of their complete restoration to function.

It can readily be surmised that with so great a latitude of incidence and with such variability of individual glandular reactivity to noxious agents, all conceivable combinations of clinical pictures are possible, once the disease process has begun. So various groupings, depending upon the particular series of glands most obviously affected, are described by various authors. Such groups are the gonads, thyroid and hypophysis; gonads, suprarenals, parathyroids; thyroid, gonads, hypophysis and suprarenals; thymus, suprarenals, hypophysis: and so on almost indefinitely.

Symptomatology.—The syndrome develops usually between the ages of twenty-five and thirty years and is more frequently seen in males than in females. Up to this age sexual and genital development are apparently normal, or only moderately delayed. Indeed, some of the patients may have already married and borne children. After the exciting etiological factor has arisen, the patient begins to suffer from fatigue after exercise or mental strain which heretofore had been subjectively well borne. Falling out of the hair; thickening, dryness and discoloration of the skin; lack of libido and sexual impotence, as well as anorexia, nausea, vomiting, various peristaltic disturbances and loss of weight, may well be the initial symptoms, either singly or in any combination. This condition may last for years. The patient shows a face free of hair, pale, dry and of a yellowish-brown color. Occasionally there is a myxedematous condition of the lower lip which looks puffy and thick and usually more or less protruded. The skin of the body is usually thick, dry and scaly, but whitish in contrast with the pigmentation of the face. The genitals are small, the scrotal sac is without tone and the testicles are extremely small. The limbs are flail-like and the rounded muscle contour is gone. There are no acromegalic features in this syndrome, although the epiphyses are united. With weakness, a certain degree of lassitude and apathy are manifested. The patient cannot bear cold and has the constant subjective sensation of cold. Mentally, the picture is one of instability, irritability and anger arising with the slightest provocation. A lack of inhibition is manifest. In those cases in which the syndrome arises soon after puberty, the voice remains high-pitched. Polyuria and polydipsia are frequently met with. Diarrhea and progressive gastro-intestinal disturbances occur; a slow pulse, low blood-pressure and vasomotor instability are also present. Murri reports acroparesthesia and erythromelalgia. Here the syndrome merges into that of the Raynaud type. The teeth frequently fall out and those that perchance remain are carious (Sourdel). Headaches and neuralgic pains in the extremities and elsewhere are common; frequently

they are so intense as to prevent sleep. While no actual muscular atrophy is seen, yet tetanoid muscle spasms are met with; the reflexes are unaltered save for the cremasterics, which are diminished. Hyperacusis and tinnitis also occur; smell is usually diminished, or may be entirely absent; nasal hydrorrhea has been reported; physical and psychical impotence usually obtain; the blood examination frequently shows a leukocytosis and eosinophilia.

Progress.—The progress and evolution of the syndrome are usually protracted over a number of years. Frequently, an intercurrent disease determines a lethal end; usually this disease is of an infectious nature as the resistance to infection is markedly diminished. Unless such interruption occurs, the gradually increasing asthenia finally determines the outcome. Drowsiness becomes more and more prominent, the progressive weakness necessitates complete rest in bed, the bedridden patient sinking lower and lower until finally he dies. There are exceptions, fortunately, in which the course of the disease has been arrested; remissions have taken place and occasional cures have been effected. Cordier and Francillon describe a remission to the point of recrudescence of libido. Byrom Bramwell reports improvement and the reacquisition of sexual potency in one of his cases. The disappearance of some symptoms, however, frequently ushers in the appearance of others. Thus, Sourdel describes the appearance of diminution of vision and hemeralopia with the disappearance of the genital symptoms and the appearance of hairy growth. A subsidiary form of the syndrome presents changes in the pigmentation of the skin with symptoms of exophthalmic goiter and eunuchoidism. Such types are reported by Sourdel, Levi and Rothschild, Faure-Beaulieu, Villaret and Sourdel. The secondary type usually occurs in the wake of an infectious disease, beginning with headache, dizziness and loss of hair, especially marked in the secondary sex regions. With these tissue changes there also occur changes in the mental sphere. The patient becomes irritable, depressed and self-centered; alternate boulimia and anorexia are exhibited. Coincidentally, the disturbances in the skin become apparent; brownish patches and sometimes vitiligo develop. With the disappearance of the secondary hair growth, the breasts atrophy and possibly exophthalmos and a slightly enlarged thyroid make their appearance. Following closely upon this, tachycardia with cardiac dilatation becomes evident; vomiting and diarrhea assist in making the patient miserable; libido vanishes; asthenia supervenes; there is chilliness with alternate colliquative perspiration. During this development the blood-pressure goes lower and lower and death at last brings relief. The development is much like the Addisonian but much slower. Still other subtypes which, together with the myxedematous characteristics of the above, evince disturbances pointing to the involvement of the pituitary gland, with genital and gastro-intestinal accompaniments, are described

by various observers (Brissaud and Bauer, Collard-Huard, Cordier and Rebattu, Renon, DeLille and Minier-Vinard).

Pathology and Pathogenesis.—A number of cases of pluriglandular insufficiency have come to autopsy (Sourdel). With great uniformity, there have been found in the glands, suspected clinically, processes of connective tissue hyperplasia, scleroses, findings that explain their dysfunction during life. The glands implicated were chiefly the thyroid, gonads, hypophysis and suprarenals. The sclerosis determined a definite functional lack, for large areas of the parenchyma of the involved glands were destroyed. In the thyroid, tuberculous nodules with connective tissue proliferation were frequently seen. Connective tissue infiltration of the liver and pancreas was noted in several of the cases. In endeavoring to account for this pathological process many theories have been advanced. Wiesel postulates that the thyroid gland bears the same relation to this interstitial process that the pituitary bears to fat deposits, based on the fact that these cirrhotic processes are never seen in hyperthyroidism but almost invariably accompany the subthyroid states.

Differential Diagnosis—*Myxedema.*—While true myxedema is more or less an entity, the myxedematous features of this syndrome form only part of the picture and arise secondarily and much more slowly than in straight-forward myxedema. Furthermore, women are much more prone to myxedema than men, while the reverse is true of pluriglandular insufficiency. The nervous and mental symptoms play a dominating rôle in myxedema, while in the pluriglandular syndrome they take a more subsidiary part; on the other hand, gonadal disturbances are of much greater importance in the pluriglandular disease than in myxedema. The blood-pictures also differ in the two conditions. The leukopenia and relative lymphocytosis of myxedema are scarcely ever seen in this syndrome. The fact that the administration of thyroid is only partially successful in combating the insufficiency syndrome as compared with its striking results in myxedema is also of great differential value.

Addison's Disease.—While pronounced pigmentation occurs in both conditions the disturbances of hairy growth are rarely seen in Addison's disease. Addison's disease is much more rapidly progressive.

Dystrophy Adiposogenitalis.—No hypophyseal tumor is demonstrable in the pluriglandular syndrome.

Infantilism.—In this condition the body is small, the bony structure is delicate, while the head is of normal size. In pluriglandular cases there is no bodily disproportion and the appearance of senility in them finds no counterpart in infantilism. The genitals do not resemble those of children but rather developed structures which have atrophied.

Thymus-Adrenal-Hypophyseal Syndrome (*Timme*).—In this condition the process begins in infancy or early youth and is based upon a presumably disturbed thymus function, as contrasted with the syndrome

under discussion. Myxedematous conditions never appear and the falling out of hair is not recorded in the Timme syndrome, though there is a deficiency of hair *ab initio*. The thymus-adrenal-hypophyseal syndromes run a protracted course usually to a recovery, while the insufficiency disease usually becomes progressively worse until death intervenes.

Interpretation and Therapy.—As has been intimated in the foregoing discussion, the prognosis of pluriglandular insufficiency is poor in spite of all our therapeutic efforts. This raises the interesting point of whether we are on the right track after all in regarding this as a disease of the glands of internal secretion. Experimental, pathological and clinical evidence preponderantly favors the view herein stated. Accepting this premise, we have two alternatives to account for the lack of specificity of our therapy, namely, that the basic disturbance of this disease may be in the disturbance of the internal secretion of the liver or pancreas, or both, whose effect we are only beginning to learn and whose therapy, with respect to the liver at any rate, is yet prenatal, or else the glandular products which we employ as therapeutic agents are too crude to supplant in physiological effect those destroyed in the body. I am inclined to think that both these factors obtain.

Be that as it may, temporary improvement is often gained and very occasionally striking results are secured by our present methods, which makes worth while their record here. We can with fair accuracy pick out from the variegated picture of this disturbance certain effects due to the lack of secretion of a certain gland. Thus, the disappearance of the secondary sex characteristics and the libido may be attributed to failure of the internal secretion of the gonads and possibly the suprarenal cortex. Small doses of the gonadal extracts, 2 gr. of the ovarian or orchitic substance, as the case may be, by mouth, twice daily, seem to have the optimum effect. This treatment may be supplemented with suprarenal cortex, 2 gr., twice daily, by mouth, often with very good effect. Gonadal therapy is taken up in greater detail in my chapters on Diseases of the Gonads. The loss of hair on the scalp, the dry, myxedematous skin, the changes in the teeth and many of the other trophic disturbances, together with the accompanying psychic changes, may be attributed to thyroid insufficiency. For this reason, thyroid substance is fed, beginning with ½ gr. daily, and gradually increasing to the limit of tolerance. It might be said in passing that thyroxin does not supplant in clinical effect thyroid substance, as it probably represents only one of the active principles of the gland and not all of them. The polyuria and general cachectic condition are probably hypophyseal in origin and for these symptoms small doses of whole gland pituitary are given, that is, ½ gr. by mouth, daily. This dosage is usually not increased as the small doses are most often the most effective. The appearance of pigmentation, hypotonus and asthenia may be interpreted as signs of suprarenal involvement (Wiesel). Clinical

experience has taught that suprarenal substance is most effective when fed in small amounts and then only for a few days at a time. The usual procedure is to give suprarenal substance, ½ gr., three times a day, four days out of each week. Adrenalin, like thyroxin, only represents one of the active principles of the gland and does not give as good clinical effects as does the whole gland substance.

Group 4 includes such conditions as hyperthyroidism with hyperadrenalism which have been considered in detail elsewhere in this work (see Chapters on Diseases of the Thyroid and Diseases of the Adrenals).

Group 5 includes pluriglandular compensatory syndromes and will be taken up in detail.

PLURIGLANDULAR COMPENSATORY SYNDROMES

General Description.—This new syndrome, first described by Timme in 1918, may be generally stated to begin in youth some years before puberty, and to go through its varying stages in about twenty years. In its incipiency, *first stage,* it presents largely the characteristics of the so-called status thymicolymphaticus, or status hypoplasticus of Bartels. There is complaint of muscular fatigability as a subjective sign with the frequent accompaniment of headache. Objectively, the case presents usually, but not invariably, an insufficient genital development, with perhaps an inversion of sex type; with a penis that emerges from a scrotal fold of labial type, or cryptorchism, or both. In the female the menses are usually delayed, the uterus and ovaries remain infantile, and there is a scarcity of pubic hair. Blood-pressure is usually low and blood-sugar content low. Enuresis is common. The white Sergent line is usually present.

In the *second stage,* that beginning at puberty, we find a continuance of the muscular fatigability or even an increase. The genitals may remain backward or even inverted in development, the pubic hair is sparse and has the distribution of the opposite sex, the male showing a horizontal demarcation, while the female shows the pyramidal type of escutcheon. Axillary hair is absent. The beard fails to develop in the male. Blood-sugar is low, usually below 0.07 per cent, and the blood-pressure is below the normal. The white adrenal line may be elicited especially after fatiguing exercise. Roentgenograms of the skull usually show a sella turcica which is small, or which may appear to be closed in by the clinoid processes. This is an important point to determine, for the later progress of the disorder presumably depends upon the capacity of the pituitary gland to become enlarged. The size of the sella turcica, therefore, plays a determining rôle in the production of the latter symptoms. The possible excessive function of the pituitary later on dominates the picture and is

conducive to a compensatory cure. X-ray of the chest frequently reveals the presence of an enlarged thymus. In some cases of extreme fatigability a pineal shadow is present. During the second stage, rapid growth in length takes place; an increase of five or six inches in a year is not infrequently noted. With this growth, fatigability increases and it is for this reason that the patient is first brought to the physician.

In the *third stage* we begin to see the results of some of the compensatory activities. This stage is usually ushered in about the twentieth year of life; growth has continued until the patient is six feet tall or over; weakness and fatigability, in spite of seemingly good musculature, are the outstanding features. The male shaves rarely, if ever; pubic and axillary hair remain as before; enlargement of the hands and feet are noticed and frontal or intratemporal headaches become an aggravating symptom; blood-pressure remains low (90 to 100, systolic); blood-sugar usually remains low, but now frequently rises as compensation takes place. The patient shows decided vagotonic symptoms. The X-ray of the skull during this stage shows a sella turcica, which, too small, gives evidence of beginning erosion of parts of its bony framework, most frequently the dorsum or the clinoids, or both. I regard this apparent increase in the size of the pituitary within an inadequate sella turcica as productive of the headaches which complicate this stage of the disease. Headaches are usually absent when the sella turcica is not of the closed-in type.

The *fourth stage* is entered upon from three to ten years later. This is the stage in which either complete compensation is produced or else the untreated case takes on the varying and various attributes produced by an enlarged pituitary body engrafted upon the earlier manifestations of a thymic state. In the compensated cases there are features of acromegalia in varying degrees and the X-ray reveals a large sella turcica. The blood-pressure and blood-sugar are normal and the headaches have disappeared. The uncompensated cases show a small and probably still closed-in sella, increasingly severe headaches and, depending upon the degree of pituitary involvement, increase of weight, increasing fatigue, drowsiness, mental torpor, perhaps petit mal or grand mal attacks and eventually a lethal termination due to intercurrent disease.

Etiology.—In practically all of our cases there have been family histories of importance in regard to endocrinopathies. Frequently parents or grandparents have shown such disturbances as diabetes, goiter, or acromegalia. A very common complaint is giantism. Collateral branches, too, show similar disturbances. There was no history of antecedent disabling disease or injury in the majority of cases. One patient, now in the second stage, had two brothers, both of whom died suddenly of unknown cause. They were both young and in each case death followed exertion. It is probable that both of these were thymic deaths. Migraine and peri-

odic headaches are common familial antecedents. Menstrual disturbances of all kinds are frequent among the female members of the family.

Discussion of Pathogenesis.—During the *first stage* we see a clinical picture which is dominated by the characteristics of the status hypoplasticus of Bartels. The anomalies have been variously credited to hypofunction of several of the incretory glands, with hyperfunction of the thymus. Tandler and Grotz, and also Tandler have ascribed many of the features of such a condition to deficiency of the gonads. In direct contradiction to their view that gonadal deficiency produces growth in height with delayed joining of the epiphyses, a case was seen in which, at the age of eighteen years, with no menstrual flow yet established and infantile sex organs, the skiagram of the long bones showed the epiphyses almost united. This patient is less than five feet tall. Weisel and Schur, and Schmorls and Ingiers have given both clinical descriptions and histological and pathological findings in such hypoplastic conditions referable to underactive or inhibited suprarenal glands. Many observers have noted the smallness of the sella turcica and our findings have been substantially in support of these observations. All of our cases showed smallness of the sella in the early stages. With such evident, diminished potential physiologic activity of the pituitary gland at the outset, the organism must of necessity come to early grief unless some corrective mechanism is soon set in motion. Many patients do succumb early; undue exertion, sudden excitement, narcosis, are all critical moments for such organizations, many of which cannot survive them. This condition is well known in persistent thymic states and it is on this basis, together with the fact that thymic shadows are present in the X-rays of many of these cases, that I conclude that the excess thymic secretion present at the normal age of puberty, delays that phenomenon, inhibits genital development and union of the epiphyses and promotes the tremendously rapid growth seen in these cases at this age (*second stage*). A failure of the adrenal-chromaffin system to keep pace with this rapid growth accounts for the great fatigability, the low blood-sugar content, the low blood-pressure and the white skin line.

Now comes the all-important *third stage*. It is in this period that the outcome of the syndrome is determined. In my opinion it is the pituitary gland which is here the critical factor. As we have seen, it is invariably enclosed in a small sella turcica and possibly even hemmed in by clinoids. Among its functions we have a blood pressor factor and a sugar mobilization factor, both of which are deficient in the patient under discussion. If the pituitary could become hyperplastic and hyperactive, with a resultant intensification of these important properties, compensation might be accomplished. In addition to this, there is the delayed puberty and sexual immaturity of these cases which must be overcome. As will be seen in the chapter on the gonads there is important evidence to show

that the pituitary gland, anterior lobe probably, exerts a decided influence on sex maturation. This places further burden upon the pituitary body in compensating these cases and furnishes additional reason for its hyperplasia. A careful study of the sella turcica pictures of these patients gives ample grounds for concluding that the hypophysis does actually enlarge at this period. A series of sella X-rays made on the same patient through the various stages of this syndrome will often show the gradual erosion of the anterior or posterior clinoids, or the floor or the dorsum, and in the final stage, a large sella with practically no clinoid processes remaining. In the cases in which no compensation is effected, that is, in which fatigability and other symptoms remain and progress, the sella shows no enlargement. Such a tendency to hyperplasia in a small cavity would of necessity, through pressure, produce a headache, an invariable accompaniment of the third stage of these compensated cases. And such a headache would continue until the bony fossa of the pituitary is eroded to sufficient size to accommodate the requisite enlargement of the gland. Clinical evidence bears out this supposition. Synchronous with the headaches other evidences of increased pituitary activity become manifest: (*a*) acromegalia, progressing with and ceasing with the headaches; (*b*) a higher blood-sugar content; (*c*) a higher blood-pressure; (*d*) diminished sugar tolerance; (*e*) beginning sexual maturity. In addition to the headaches in these cases there is often adiposity, mental and moral deficiency, petit mal seizures and other manifestations.

Curiously enough, the feeding of pituitary substance disposes of many and at times all of these symptoms. But if the feeding is diminished or stopped, the symptoms reappear. It seems analogous to thyroid feeding in myxedema. One case, which gives a typical early history and seems uncompensated to-day at the age of forty-four, still shows the abnormally small sella turcica with a clinical picture of abnormal bony structure much resembling Paget's disease. On pituitary feeding this case is improving rapidly in its features of fatigability, headaches and heaviness of the extremities.

The *fourth stage* of this disease is ushered in by a gradual cessation of the fatigue, amelioration of the headaches, restoration of the normal blood-pressure, and normal sugar content of the blood. However, the adventitious signs of the pituitary disturbance remain. Hence the fully compensated cases may show acromegalia, more or less marked, and this acromegalia is not to be taken as a diseased condition needing treatment, but simply as the hallmark of a process that has come to a stop, a self-limited process. It is analogous to the compensatory hypertrophy of the heart in valvular disease, in that the enlargement, per se, needs no treatment. To avoid unpleasant symptoms, in both cases, the patient must live within certain limits of exertion and stress. The cases in the fourth stage that do not go to full compensation are those in which we either

find a sella turcica which did not enlarge (perhaps because there was no spontaneous effort of the pituitary to become hyperactive), or in which the enlargement of the sella did take place, yet the hyperactivity of the pituitary was insufficient to compensate. These uncompensated cases present a fertile field for therapy as it is often possible to deviate them, by proper pituitary feeding, from the state of increasing fatigability and torpor to which they are inevitably progressing.

Treatment.—The treatment of these cases in any stage is, in the writer's experience, satisfactory. The important point to remember is the probable nature of the process of compensation which the organism is endeavoring to carry out. This would make one believe that suprarenal therapy is indicated throughout on account of the patent deficiency of the suprarenals in these cases. And yet in our hands administration of suprarenal products is often disappointing. The whole gland perhaps has given better results than epinephrin, although the latter, either hypodermically or (even against the dictum of the pharmacologists that it is inert when given by mouth) per os in larger doses is good to tide over exceptionally bad days of fatigue and exhaustion. But the prime agent, almost specific, is pituitary gland in some one of the varied forms. Whole gland feeding in fairly large doses (2 to 3 gr. three times daily) may be given in appropriate cases. But usually the dosage should begin with relatively small amounts, ¼ to ½ gr. doses, every other day, or daily, and then worked up to tolerance. Large doses will frequently aggravate the headaches and thus defeat their own purpose. Small doses are frequently the most effective. Occasionally, pituitrin hypodermically (obstetrical), 0.50 to 1.00 c.c. per day, or every other day for one or two weeks at a time, is excellent as supplementing the feeding of pituitary substance. In cases with pronounced genital delay, anterior lobe pituitary substance, by mouth or hypodermically, is of benefit. In those cases with vagotonic symptoms, hypo-acidity and symptoms resembling gastric ulcer, atropin in doses to physiologic tolerance yields results. The pituitary feeding alone produces highly satisfactory results in many cases. Under its use the headaches disappear, the fatigability diminishes, the blood-sugar content and blood-pressure increase and the case goes on to recovery. Gradually the pituitary feeding can be decreased and finally discontinued. In older cases, in which the sella turcica persists in remaining small, constant feeding would seem to be necessary; at all events, the patients relapse as soon as treatment is stopped. The patients themselves reach that point of accuracy of judgment in feeding the gland to themselves that they can determine the size and frequency of the dosage necessary to maintain them comfortably.

Group 6 includes the pluriglandular antagonistic syndromes, so called for want of a better name, and serves to designate certain paradoxical cases which not infrequently confront the clinician. They are too vaguely

understood for the most part to admit of a definite description and outline of therapy, but it is felt that they should be mentioned in a book of this kind if for no other reason than to stimulate their further study.

Symptoms commonly supposed and generally accepted to be evidence of increased secretion of a certain gland will sometimes occur in the same patient with symptoms quite as properly ascribed to undersecretion of that gland. For instance, in the milder forms of disturbed thyroid function, a rapid pulse, increased basal metabolism, loss of weight, slight lagophthalmos and exophthalmos may be associated with loss of hair, brittleness of the nails, dryness of the skin, great fatigability and lack of resistance to cold. Occasionally, the reverse is true in which a mild hypothyroid state may be associated with rapid growth of hair and nails. I have recently had under my observation a case of unmistakable myxedema with a basal metabolism ranging from plus 80 to plus 95 on three separate tests. Typical hypopituitary adiposity is sometimes associated with prognathism and other signs of acromegalia. In the gonadal sphere we frequently see increase of libido and sexual appetite associated with the menopause.

These examples serve to illustrate the nature of the cases which are sufficiently distinct in their symptomatology, yet possess a sufficient number of points in common to deserve a separate heading. They undoubtedly represent a heterogeneous mixture, yet we cannot pass them by unnoted. In this group the most rational avenue of therapeutic approach is to attack the predominating symptom, despite the paradoxical lesser ones, but this must be done with caution and is at best a trial and error process.

Group 7 includes the milder forms of the above disturbances and needs no particular elucidation. Their diagnosis and therapy are along the lines already laid down for their more pronounced counterparts. Needless to say, it is in this class that our most gratifying results are obtained.

REFERENCES

Agnostini. Infantilismo Distrofico e Infantilismo Mixedematoso du Eredopellagra, Riv. d. patol. nerv., 2, 1902.

Bartel, J. Uber die hypoplastische Konstitution und ihre Bedeutung, Wien. klin. Wchnschr., xxi, 783-790, 1908.

——— Status Thymicolymphaticus and Status Hypoplasticus, Wien. and Leipzig, F. Deuticke, 1912.

Brissard and Bauer. Un cas d'infantilisme reversif avec autopsie, Bull. et mém. Soc. méd. d. hôp. de Paris, Series 3, xxiv, 39-41, 1907.

Claude, H., and Gougerot, H. Sur l'insuffisance simultanée de plusieurs glandes à secretion interne, Compt. rend. Soc. d. biol., Paris, lxiii, 785-787, 1907. Ibid.

Claude, H., and Gougerot, H. Syndromes pluriglandulaires, Gaz. d. hôp., Paris, lxxxv, 897-904, 1912.

Collard-Huard. De l'insuffisance ovarienne envisagée dans ses rapports avec l'insuffisance thyroidienne, Paris, Jouve et Cie., 1911.

Cordier and Francillon. Un cas d'infantilisme avec syndrome pluriglandulaire, Lyon méd., cxvi, 25-31, 1911.

Cordier, V., and Rebattu, J. L'infantilisme regressif or tardif, N. Inconog. de la Salpêtrière, Paris, xxiv, 448, 1911.

Faneau de la Cour, F. V. Du feminisme et de l'infantilisme chez les tuberculeux, Paris, 1871.

Faure-Beaulier, F., Villaret, M., and Sourdel, M. Syndrome pluriglandulaire, Presse méd., xix, 691-693, 1911.

Hartoghe, E. Diagnostique de la possibilité d'une reprise de croissance, Bull. Acad. roy. de méd. de Belg., Brussels, Series 4, x, 564-569, 1896.

Levi, L., and Rothschild, H. Les petits signes d'insuffisance thyroidienne, Gaz. d. hôp. d. Paris, lxxx, 879, 1907.

Lewandowsky. Handbuch d. Neurol., Berl., J. Springer, iv, 1913.

Murri, A. Sur un case d'insuffisance pluriglandulaire, Riforma. med., xxvii, 85-91; 113-118, 1911.

Poncet, A., and Leriche, R. Tuberculose inflammatoire et glandes vasculaires, sanguines, Lyon méd., cxvii, 39-57, 1911.

Renon, L., DeLille, A., and Monier-Vinard, R. Syndrome pluriglandulaire par hyperactivité hypophysaire, Bull. et mém. Soc., méd. d. hôp. de Paris, Series 3, xxvi, 1037-1039, 1909.

Schur, H., and Wiesel, J. Uber das Verhalten des chromaffinen Gewebes bei der Narkose, Wien. klin. Wchnschr., xxi, 247-248, 1908.

Sourdel, M. Contributions à l'étude anatomo-clinique des syndromes pluriglandulaires, Paris, 1912.

Tandler, J. Infantilism, St. Paul Med. Journ., x, 1-9, 1908.

——— Uber den Einfluss der inner-secretorischen Anteile der Geschlechtsdrusen auf die aussere Ercheinung des Menschen, Wien. klin. Wchnschr., xxiii, 459-467, 1910.

Tandler, J., and Gross, S. Uber den Einfluss der Kastration auf den Organismus, Wien. klin. Wchnschr., xx, 1596-1597, 1907.

——— Arch. f. Entwcklngsmechn. d. Organ., xxvii, 36-61, 1909.

——— Untersuchungen an Skopzen, Wien. klin. Wchnschr., xxi, 277-282, 1908.

——— Uber den Einfluss der Kastration auf den Organismus, Arch. f. Entwcklngsmechn. d. Organ., xxix, 280-324, 1910; Part 2, 236-251.

Timme, W. Endocrinopathic Inheritance, Journ. Am. Med. Ass., lxvi, 1438-1441, 1916.

——— A New Pluriglandular Compensatory Syndrome, Endocrinology, ii, 208-240, 1918.

Wiesel, J. Zur pathologie des chromaffin Systemes, Virchow's Arch. f. path. Anat., etc., clxxvi, 103-114, 1904.

DEVELOPMENTAL DISEASES

CHAPTER XVIII

DEVELOPMENTAL DISEASES

GEORGE BLUMER

The diseases gathered together under this heading constitute a somewhat heterogeneous group for the reason that the only point they have in common is the fact that they are inborn and often, though not necessarily, hereditary. For this reason it would seem as though their description in a work on treatment was almost superfluous. This is not strictly the case, for, while it may not be possible to remedy anatomical developmental defects, it may be feasible to aid defective physiology and it is frequently possible to produce a measure of symptomatic relief.

The chapter cannot be regarded as complete but contains descriptions of some of the better known and commoner conditions. It hardly seemed desirable to include in a work of this scope the management of certain well-known inborn conditions such as feeble-mindedness, although certain anatomical lesions with which this is incidentally associated are considered.

INFANTILISM

There is some difference of opinion as to the exact definition of infantilism but it is perhaps best described as an "arrest of development at a childish phase." The patients are usually of childish size and proportions, of childish mentality, and show failure of development of the secondary sexual characteristics.

According to Borchardt's classification patients with infantilism may be grouped under the following types:

1. Hereditary infantilism due to inherited abnormal growth tendency.
2. Infantilism from germ damage, that is, the effect of lead, alcohol or X-ray on the parental germ cells.
3. Infantilism of Endocrine origin.
   - *a.* Dysthyrogenous.
   - *b.* Hypophyseal.
   - *c.* Pluriglandular.

4. Dystrophic Infantilism.
   a. From infection either congenital or acquired early with syphilis, tuberculosis, leprosy, hookworm, malaria, pellagra or echinococcus disease.
   b. From underfeeding or improper feeding in infancy or early childhood. Intestinal infantilism and juvenile alcoholism may be included in this group.
   c. From congenital cardiac or vascular disease or heart disease acquired at an early age.
   d. Pancreatic infantilism really belongs in this class as it is due to lack of the external secretion of the gland.

Treatment.—Treatment is much more hopeful in some forms of dystrophic (symptomatic) infantilism than it is in the other types. Where the condition is due to lack of food or improper food, a certain amount of amelioration may be expected from feeding correctly as to quantity and quality. Where it is due to juvenile alcoholism the correction of the habit may, if carried out early enough, lead to some improvement. Little improvement can be hoped for in the patients with severe cardiac or vascular changes. The pancreatic type may be greatly improved by appropriate pancreatic medication (see Diseases of the Pancreas, page 752).

In the infantilism of thyroid disease (cretinism) striking results have been obtained from the administration of thyroid extract (see Diseases of the Thyroid, page 120), but the treatment of hypophyseal infantilism with pituitary extract has so far been quite disappointing. It should, however, be given a trial.

PROGERIA

Progeria is a rare condition in which a combination of infantilism and senilism is found in the same individual. The subjects of the disease are dwarfs in size but present many of the aspects of senility. The skin is atrophic and loose-fitting like the skin of old people, the features are sharp, the expression immobile and hair is lacking or extremely sparse and downy. The musculature is poorly developed and this with the prominent joints adds to the resemblance of old age. The mentality is often in advance of the age of the patient. The veins are large and conspicuous. The disease begins in early childhood and progerians usually die of old age about the age of eighteen.

The exact nature of the disease is in doubt. From a study of the skeleton Arthur Keith regards the condition as the opposite of acromegalia, but the sella turcica is little if any smaller than normal. Hastings

Gilford, who has studied the disease during life, rather doubts its pituitary origin. C. W. Rand suggests that it may be a polyglandular syndrome.

Treatment.—No treatment has been successful. In Rand's patient feeding with anterior pituitary had no effect whatever. It is doubtful whether satisfactory therapeutic results can be obtained until more exact knowledge of the nature of the disease has been obtained.

MONGOLISM

The term "mongoloid" was first applied in 1886 by Langdon Down to designate a type of developmental defect which has also been called "Mongolian idiocy" and "Kalmuck idiocy." The subjects of the condition present a peculiar facies, oriental in type, with an abnormal skull morphology, disturbances in the bones and joints, lack of both physical and mental developmental capacity and decreased resistance to infections.

The exact nature of the process is still in doubt. Timme and others regard it as an endocrine disturbance, basing their views on certain changes in the configuration of the sella turcica and certain features of hypothyroidism, such as thick features, pot belly, frequency of umbilical hernia, and deficient circulation. Other observers with wide experience regard it as a developmental disturbance rather than a disease. Dollinger thinks it more likely to occur in the children of old parents. It has been claimed to be more frequent in the late than in the early children of a family.

Mongoloids present an extraordinary resemblance to one another so that parents visiting an institution where there are many of them may not be able to pick out their own child. The face is flat, the nose is broad and projects but little, the lid slits slope downward and inwards like those of the yellow races, and many of the patients have epicanthus. The eyes are widely spaced and set in shallow orbits and the eyebrows are sparse. Blepharitis is common and nystagmus and strabismus are not unusual. The mouth is small and gaping and the tongue is often visible, larger than normal and deeply fissured, the so-called "lingula scrotalis." The voice is rough or squeaking. The teeth are often small and very irregular. The hands are plump and the digits, particularly the thumbs, are often stubby. The pulse is small and the blood-pressure is low. The general state of nourishment is usually good but the stature is subnormal, the muscles are hypotonic and feeble and the belly is prominent. The mentality is always defective, all grades of feeble-minded individuals from extreme imbeciles to high-grade morons being represented. The temperament is usually a happy one and mongoloids are frequently fond of music and rhythmic movements. Growth seldom progresses after the age of

fifteen, and three-quarters of the patients die before puberty, usually from acute respiratory infections.

Treatment.—In the hands of most observers treatment has been without avail. Timme claims to have obtained some benefit from hypodermic injections of extract of the anterior lobe of the pituitary combined with whole gland feeding and small doses of thyroid extract. He has not yet published his final results. These patients are capable of a limited amount of rudimentary education and can be trained to a certain degree of manual dexterity. They are practically never able to cope successfully with the conditions of the outside world and must be maintained in institutional surroundings.

AMAUROTIC FAMILY IDIOCY

There is a group of familial degenerative eye diseases, with or without accompanying cerebral degeneration, of which amaurotic family idiocy is the best known example. The group includes the infantile and juvenile types of amaurotic family idiocy and familial macular degeneration with or without dementia. The diseases of this group merge gradually into one another and the etiology of all is obscure, though many writers assume a toxic origin. In clean-cut cases of amaurotic family idiocy there is extensive degeneration of the nerve cells throughout the cerebrospinal system.

Amaurotic family idiocy generally attacks eastern Jews, and is characterized by the appearance in apparently healthy infants, usually at about the age of two or three months, of increasing muscular flabbiness and weakness with arrest of mental development, apathy, and increasing blindness. Hyperacuity of hearing is common and general hypersensitiveness is sometimes present. The course is progressively downhill and invariably ends in death. The ophthalmoscope shows a central cherry-colored spot in the macular region surrounded by a grayish zone of infiltration and accompanied by gradual optic atrophy.

Treatment.—Treatment is without avail as the condition is due to congenital anatomical deficiencies in the nervous system.

ACHONDROPLASIA

Achondroplasia is a congenital disease characterized by defective development of cartilage. It is also known as chondrodystrophia fetalis and fetal rickets. It is probably mechanical rather than chemical in origin and due to a small amnion compressing the fetus in the early stages of its development. It is occasionally hereditary.

The lesions of the disease produce a well-known form of dwarfism. The bones of the extremities are too short, the third and fourth fingers of the hands diverge more widely than normal (trident hand), the pelvis is small in proportion to the trunk, the basis cranii is shortened, the head is brachycephalic and the vertebræ are wedge-shaped. The resultant individual is a large headed, snub-nosed dwarf with a relatively long trunk, very short arms and legs, trident hands and a loosely fitting skin. The intelligence is unimpaired and the sexual functions tend to be hyperactive.

Treatment.—There is no treatment which has any effect on the disease. In females who are subjects of it the deformed pelvis must not be forgotten, as in case of pregnancy cesarian section is generally necessary.

HEREDITARY DEFORMING CHONDRODYSPLASIA

This is a developmental condition which has also been described as "multiple cartilaginous exostosis" and which is probably not nearly so rare as was believed at one time. The disease has a very definite hereditary tendency and is characterized by the development of cartilaginous exostoses, usually on the long bones, but not infrequently on the flat bones. These outgrowths are frequently not noted until adult life, though in some instances they have been observed at birth and they are probably present during fetal life.

The condition is more common in males than in females and is associated with secondary distortions and deformities of the skeleton due in part to retardation of growth, in part to overgrowth. In some situations the cartilaginous growths may themselves interfere with normal bone development. The patients may only become aware of the disease when the cartilaginous exostoses reach a size which causes mechanical interference with joint or other motion, or when infection of overlying bursæ or the bone itself or secondary malignant neoplasms become apparent. The researches of Underhill, Honeij and Bogert have shown that definite disturbances in calcium and magnesium metabolism occur, increased excretion of calcium and magnesium in the progressive stage of the disease and in the stabilized stage increased magnesium excretion.

Treatment.—When the disease occurs in families an attempt should be made to discover those individuals who have exostoses at as early an age as is possible. During the early stages a restriction of the calcium and magnesium intake may hold the process in check. When the exostoses are discovered at a later date their surgical removal may be indicated for one of three reasons: interference with function, infection of overlying bursæ or the exostoses themselves, or malignant degeneration.

OSTEOPSATHYROSIS IDIOPATHICA

There is more than one congenital condition of the osseous system associated with abnormal fragility of the bones, but the commonest form is that known as "fragilitas ossium" or "osteogenesis imperfecta." This is a condition which is probably always due to an inborn defect but which may not become apparent until late childhood or even adult life. For this reason some writers speak of osteogenesis imperfecta congenita and osteogenesis imperfecta tarda.

The etiology of the condition is unknown. Brauer describes it as a transmissible constitutional anomaly of the derivatives of the mesenchyma but is not able to put his finger on the exact cause. Some think that endocrine deficiencies or disorders underlie the process but there is no convincing evidence that this is the case. Still others blame lack of certain vitamins. Bookman has shown that in active cases the calcium retention is below normal.

The clinical picture of the disease presents in many instances nothing beyond the history of repeated fractures from trivial causes and the deformities resulting from these, though some patients have a large head and a relatively small chest. In certain patients there are peculiar associated phenomena, particularly blue scleroties and otosclerosis. More rarely a tendency to luxations and subluxations, zonular cataract, macular atrophy of the skin, syndactylia, cleft palate and congenital heart disease have been noted. The teeth may develop late; in Vanderveer and Dickinson's case they were translucent. The bones are often normal in length but are thin and show defective calcareous development. If the patients survive beyond the age of twenty the process generally ceases.

Treatment.—It is generally conceded that glandular therapy and arsenic are valueless. There is difference of opinion as to the use of cod-liver oil, phosphorus and calcium. Hess uses either a mixture of phosphorus 0.01 gm. in 60 c.c. of cod-liver oil or a mixture of pure tribasic calcium phosphate 6 gm. in cod-liver oil 60 c.c. In either case the dose is 4 c.c. twice daily. Czerny reports good results from 100 c.c. of raw carrot juice daily.

The great object of treatment is to protect patients against trauma so that new fractures will not occur. When, however, fractures occur in spite of this they are to be treated as any other fracture. They usually heal well but may leave marked deformities and in some instances these may be so pronounced as to demand a corrective osteotomy. This, however, should be undertaken only after deliberation, as healing may be very slow.

It is to be noted that the treatment is entirely symptomatic and satisfactory therapy will not be forthcoming until we have a much clearer conception of the nature of the disease.

OSTEOSCLEROSIS FRAGILIS CONGENITA

This condition is also known as Albers-Schönberg disease and marble bones (*marmorknochen*). It is usually due to an inborn anomaly which is characterized by a high blood calcium (Schulze) and an excessive deposit of this salt in the bones and at times in the ligaments and on the surface of the blood-vessels. The bones appear in X-ray pictures as deep black shadows. There may be thickening of the processes of the sella turcica and narrowing of the foramina of the skull, at times with optic atrophy. Severe and fatal anemia may occur. As in osteopsathyrosis the bones are unduly fragile and there is generally a history of multiple fractures.

Treatment.—Little is to be done in the way of treatment beyond the handling of the fractures along the usual surgical lines. The cause of the calcium retention is not known.

MICROCEPHALUS

This is a developmental anomaly characterized by defective cerebral development associated with imperfect cranial development. It is frequently due to intra-uterine cerebral vascular abnormalities but these are not always present. Microcephalic individuals are often found in side shows, usually labeled as the "missing link." They are undersized, mentally defective individuals who have a low receding forehead, a flattened occipital region and a small low cranium.

Treatment.—It would hardly seem necessary to discuss the treatment of a condition which from its very nature appears so hopeless were it not for the fact that the operation of craniotomy, first suggested by Lannelongue in 1891, is still discussed in textbooks on surgery. The operation was proposed on the assumption that cerebral development is retarded on account of premature synostosis of the skull sutures. There is little to support this view at present. Beneficial results seem to follow the operation at times. Wullstein and Kuttner quote Lowenstein's figures which show a mortality of 17 per cent and 48 per cent with definite improvement. In view of the possibility of a certain amount of spontaneous improvement in the mental condition these results must be taken *cum grano salis*. Certainly the operation is not one to be undertaken lightly.

OXYCEPHALIA

Oxycephalia is a developmental disease of obscure etiology characterized by premature closure of the sutures of the base and posterior

portion of the skull with a pushing upward of the vertex by the growing brain. This results in the deformity which has been described as "tower head," or "steeple head." The disease has also been called acrocephalia, scaphocephalia and hypsicephalia.

The condition occurs in two forms, one in which the head only is affected, and one in which there is associated syndactylism. The characteristic features of the first type are:

1. A very high forehead with a gradual slope to the vertex, a pointed instead of a rounded or flattened vertex, feebly marked superciliary ridges, an uplifted hairy scalp and depressed ears.
2. Eye signs, consisting of exophthalmos usually associated with nystagmus and often accompanied by squint.
3. Defective vision, due to papillitis and secondary optic atrophy. This is not invariably present. Myopia is common.

In the second type of case a fourth sign is present, namely, syndactylism in varying degrees. In both types the X-ray picture of the skull shows, in addition to the characteristic changes in shape, characteristic digital markings or dimplings, especially in the frontal area.

Treatment.—These patients frequently have no symptoms except progressive loss of vision, but at times headaches or even convulsions may occur. These are evidences of intracranial pressure and should be considered in the same light as the papillitis. There is nothing to be gained by temporizing with drug therapy and the chief and only indication is removal of the intracranial pressure as promptly as possible after the first evidences of visual deterioration. This can only be done surgically, and a bilateral subtemporal decompression is indicated. This may result not only in saving good vision but, if the disease is recognized early, in preventing the full development of cranial deformity.

VASOMOTOR AND TROPHIC DISEASES

CHAPTER XIX

VASOMOTOR AND TROPHIC DISEASES

WALTER R. STEINER

RAYNAUD'S DISEASE

Raynaud's disease is a functional disease of the blood-vessels, chiefly occurring in the extremities but occasionally seen in the internal parts, characterized by a persistent ischemia or a passive hyperemia which results in a disturbance of function or a loss of vitality, with necrosis, of the part or parts affected.

It is a comparatively rare disease affecting mostly women in the second or third decades, although no age is exempt. Several members of the same family may be affected and it is seen especially among neurotic and hysterical patients. Damp and cold weather appear to favor its occurrence. The first change is that of local syncope which comes from a spasm of the arteries and arterioles, causing an ischemia of the part or parts involved. Within an hour or two active hyperemia may be observed, but more commonly an intervening period of asphyxia is seen, the arteries and arterioles being widely dilated. It is at this stage that the pain begins. In the last stage necrosis or gangrene is seen if the circulation does not become reëstablished. In the mild forms the vascular disturbance is similar to chilblains and the hands alone may be involved, causing the appearance of a "beefsteak hand," or a single finger may be attacked. In the more severe form the cyanosis may persist, ending in the necrosis of the pad of one finger and the terminal inch of another. When these necrotic pads separate, no more attacks may follow or a recurrence may be noted in a year or two. In the still more severe form the tip of the nose and ears, and the fingers and toes may be implicated, and the attack may be accompanied by pain of great severity. The resulting gangrene may require the loss of fingers and toes, the edge of both ears and the tip of the nose. The chin, lips, nates and eyelids may also be attacked. The disease consequently may be divided in its clinical course into three stages: in the first the vasomotor symptoms predominate; the second is characterized by marked trophic disorders; while in the third gangrenous sloughs or necroses are seen, which, when detached, cause the symptoms to subside after local healing.

Treatment.—The general health of the patient must be looked after and kept in as good condition as possible. If cold weather brings on the attack, the patient should be advised to seek a warm climate during the winter months. Massage, hydrotherapy and electricity, in both its galvanic and high frequency forms, have been of service in many instances. During the attacks the pain may be relieved by the hot-water or hot-air bath. The method of stasis or hyperemia, as first suggested by Cushing, has been at times found useful. By it a semielastic or rubber bandage is made to compress the arm until venous stasis ensues, care being taken not to interfere with the arterial supply. Frequently the bandage can only be borne for a few minutes, but its use for three or four times daily is often beneficial. Pyramidon, antipyrin, phenacetin and aspirin have yielded good result, in the order named, with rest. Sometimes morphin or opium in other forms alone relieve the pain. After the onset of gangrene the treatment is wholly surgical.

ERYTHROMELALGIA

Erythromelalgia is a chronic disease which usually affects one or more extremities and is characterized by pain, redness and local fever in the part or parts affected. The symptoms are usually aggravated if the parts hang down.

As the name implies, it signifies a painful red extremity and was first described and named by Weir Mitchell in 1872. He gave an accurate clinical picture of this rare disease. Males are more often affected than females and the lower extremities are more frequently involved than the upper. The malady may cause a swelling of the lower leg or forearm which rarely extends above the elbow or knee, although the pain may reach the hip or shoulder. The redness varies in color from a deep pink to a violet red and the pain which is an almost constant accompanying symptom is either burning or stabbing in character. Sweating is commonly seen and an atrophy of the affected muscles may occur, but gangrene is never observed.

Treatment.—This affection is very resistant to treatment. An excision of the nerves of the part affected has been successfully tried in some instances where the pain was limited to a single nerve territory, but in one of Weir Mitchell's cases gangrene of the foot followed such an excision. Protracted rest, six weeks or more in duration, often relieves the pain and congestion, and should be tried in every instance. Massage frequently is beneficial, as well as some form of hydrotherapy. Electrical treatment in various forms and radiant heat have also been employed.

SCLERODERMA

Scleroderma is a subacute or chronic disease, mostly the latter, which is characterized by a peculiar hardening and rigidity of the skin, occuring in circumscribed or diffuse areas.

The changes in the skin may be preceded for a variable period of time by paresthesias (cold, numb, painful sensations or pruritus) and by cyanosis. Vague rheumatoid pains in the articulations or in the different muscles of the trunk or extremities may also be additional symptoms in this prodromal period. Then the three successive stages of edema, induration and atrophy follow which mark the development of the disease. The first stage, however, is usually absent. The disease is generally of chronic form and may continue for years. Recovery may be noted, a cessation of the symptoms may be seen or death may ensue from a pulmonary or nephritic complication. A pigmentation of the skin of the affected areas may be an accompanying phenomenon. In the variety known as sclerodactylia the fingers are symmetrically involved, becoming successively deformed, shortened and finally atrophied. Females are much more apt to be affected than males and the disease may be seen at any age. The skin of the face, of the neck, the upper half of the trunk and of the upper extremities, especially the hands, are the areas of predilection. In the diffuse cases a large part of the body may be implicated. The parts of the skin affected present a smooth, glistening, hard, mottled surface.

Treatment.—In the treatment of this disease many drugs have been empirically employed, owing to our ignorance of its etiology. Some of the cases also have spontaneously recovered with no treatment. Good results have been recorded from endocrin gland therapy, the thyroid and pituitary preparations being especially utilized. Massage is indicated as it softens the skin and apparently promotes nutrition.

PATHOLOGICAL OBESITY

Pathological obesity is the morbid deposition of fat in the body. The differentiation of its varieties presents difficulties, "for they are not only closely related, but essentially identical, being only variations of a common morbid process." For clinical convenience, however, Lyon's classification appears to be the best; he divides its types into the following subdivisions:

1. **Adiposis Dolorosa.**—It was first described by Dercum in 1888 as a disease developing in middle life, although instances in both extremes

are on record. A history of alcoholic excesses is not uncommon and most of the cases have been seen in the female sex, the disease generally developing on a neuropathic basis. In at least two instances heredity played a factor, as in Cheever's case a father and a sister were affected, while in Hammond's the affection occurred in two sisters. Most of the cases in women came on at the menopause or shortly thereafter. The adiposity may be diffuse or circumscribed, and generally develops in a patient already fat in irregular nodules within the subcutaneous tissue. These masses may vary in size from 2½ to 10 cm. in diameter, are very tender and edematous on palpation and may be the seat of spontaneous and severe pain. They soon harden and become less painful. Asthenia and psychic manifestations are also associated symptoms, the latter varying from simple apathy to actual dementia. After an insidious onset remissions and exacerbations are the rule.

2. **Nodular Circumscribed Lipomatosis.**—These swellings are fairly common and may be accompanied by pain along with the accessory features of asthenia and psychical changes. They vary much in size and may be most wide in their distribution.

3. **Diffuse Symmetrical Lipomatosis of the Neck.**—This condition has been also called adenolipomatosis and is seen as a fatty infiltration, simple or lobulated, of the subcutaneous tissues of the neck. Males are more liable to be affected than females. Little discomfort is caused by these tumors which may also occur elsewhere.

4. **Pseudolipoma.**—Pseudolipoma is a swelling seen in hysterical patients and named from them by Charcot "hysterical edema." A so-called blue and white variety has been described.

5. **Cerebral Adiposity** (*dystrophia adiposo-genitalis, Frölich*).—This condition will be discussed under its appropriate heading.

Treatment.—As the endocrin system appears to have an important bearing on these diseases, every patient should be carefully investigated for an endocrin disturbance. Unquestionably thyroid extract has had a beneficial effect in the treatment of adiposis dolorosa, and aspirin and the salicylates have been useful for the pain. Rest, diet, massage and hydrotherapy have also yielded satisfactory but temporary results. The surgical removal of encapsulated fatty tumors in the other varieties of pathological obesity is to be recommended.

PROGRESSIVE LIPODYSTROPHY

Progressive lipodystrophy is a disease characterized by a symmetrical, progressive and almost complete disappearance of the subcutaneous fat from the head, face, neck, upper extremities and trunk.

It was first described by Arthur Simons of Berlin in 1911 and has since been elsewhere reported, so that now it has been seen in at least 26 instances. The affection preponderates in females, as out of these 26 cases only 2 were found in the male. Some years after the onset of the facial wasting, there is an increase in the size of the buttocks. The onset is always insidious, without any marked symptoms, although, in the early stages, there may be vague aches and some malaise, which are later followed by a sensation of chilliness, slight nervousness and hyperidrosis. The skin over the affected regions shows, when examined, an almost entire absence of fat in the subcutaneous tissues.

There is no known treatment.

FACIAL HEMIATROPHY

Facial hemiatrophy is a slow progressive emaciation of the skin, the subcutaneous tissues, the bones and finally of the facial muscles. As the name implies only one side of the face is usually affected.

Women are much more frequently attacked than men and the left side of the face is the more commonly involved. In most of the cases, the onset is seen in childhood or youth, so a congenital anlage appears probable. Indeed, in one instance it was accompanied by acromegaly and a congenital absence of one kidney. It is due to a disease of the trigeminal nerve on the affected side, and in the only careful autopsy on record the terminal stage of an interstitial neuritis was found from the origin to the periphery of all the branches of that nerve. The onset is usually insidious without any subjective symptoms but sensory and motor symptoms in the region supplied by the fifth nerve are at times observed, along with hyperesthesias, paresthesias, spasm of the masseter muscle, neuralgic pains or epileptiform convulsions. The hair over the affected area, as well as on the scalp, may turn white or fall out, diffusely or in patches. Although the sebaceous glands cease their activity, yet the sweat glands continue to function while the skin becomes hard and rough, resembling scleroderma. A twitching or drawing sensation of the skin may be complained of, but the skin sensations remain normal as well as the reflexes, although the vasodilator reflex on the affected side may be missing. The muscles of mastication may become weak, but there is no noticeable impairment of the facial muscles. The half of the tongue and the soft palate on the affected side may eventually become markedly atrophied and there may be a wasting of the facial bones so that finally the alveolar process becomes involved and the teeth drop out. The course may be slow and progressive at first, then stationary or show spontaneous improvement.

There is no treatment to check the course of the disease. In some

cases paraffin injections have improved the patient's appearance, but are not to be recommended.

MILROY'S DISEASE

Milroy's disease is a hereditary condition characterized by persistent edema of the legs. It was first described by Milroy of Omaha, Nebraska, in 1892, and since then has been occasionally reported. In the family Milroy described it affected nearly 20 per cent or 22 individuals among 97 persons in 6 generations.

Males and females are equally affected and the patients are usually in good health. No evidences of venous thromboses or lymphatic obstruction have been found. The edema may appear shortly after birth or not until puberty or even not until adult life, but once established it is permanent. It may stop at the ankles, but usually extends to the knees and in long-standing cases may reach the thighs. It is painless, increases on standing, and may become hard and brawny. The attacks may come on acutely with fever.

Treatment.—Careful bandaging is the only efficient means to keep the swelling in check. In the acute attacks opium may be required for the pain as well as a soothing lotion for the legs.

TROPHEDEMA

Trophedema is an area of swelling of the skin and subcutaneous tissue which may be more or less sharply localized. It is due to a faulty nerve action and may be seen (1) secondary to motor paralysis; (2) from peripheral nerve lesions; (3) from psychic influences; or (4) as angioneurotic edema.

In (1) it results from a loss of rhythmic contraction in the paralyzed part which leads to an engorgement of the capillaries and a subsequent exudation in the tissue spaces. The lymph flow is also interfered with in this condition. In (2) any peripheral nerve lesion will cause it in a manner similar to (1). In (3) hypnotic influences, not yet explained, have been frequently shown to cause vesication. (4) Angioneurotic edema is a sharply defined circumscribed area of edema which may be several inches in diameter. It may come on with great and alarming rapidity and disappear just as rapidly in one area only to reappear in another just as suddenly. The affection is more common under twenty, but may be seen at any time from infancy to old age, although it is less frequent with advancing years. It is more common in women than men and in the well-to-do than in the poor. It has a familial tendency and

has been traced through many generations. The neuropathic type is chiefly affected. The swellings may be seen in any of the soft parts but are more apt to affect the skin and mucous membranes. If the skin is involved, the face and extremities are especially liable to be attacked, while of the mucous membranes the lips, tongue, nasal mucosa, larynx and intestines are the most prone to be affected. The cutaneous swellings are well defined with sharp edges and generally pit slightly or not at all on pressure. Pain is usually absent, but a sense of tension may be present. Edema of the glottis thus induced may be fatal. Colic may be seen when the intestines are involved.

The *treatment* is most unsatisfactory. For neurotic patients hygienic measures sometimes are beneficial. If the patient is hypersensitive to a food protein, it should be stricken from the diet. Colon irrigations have been beneficial at times. Occasionally the patient has recovered spontaneously after many drugs have been tried. Adrenalin hypodermically may relieve the acute swelling. Osler reports good results in some instances from increasing doses of nitroglycerin. He has given this drug in these cases until its physiological effect is produced.

HEREDITARY HEMORRHAGIC TELANGIECTASIA

This is a hereditary affection, familial in type, which manifests itself in telangiectasias or dilatations of the capillaries and venules, appearing on the skin of the face, hands and other parts of the body, the mucous membranes of the cheek, nose, lips and tongue and giving rise to profuse hemorrhages either spontaneously or as the result of trauma.

The bleeding may occur at any season. Its distribution among the sexes is about equal and either sex may transmit it. The most common situations for the telangiectasias are on the nasal and buccal mucous membranes or on the mucocutaneous junction of the lips. They may appear at an early age, but generally they do not attain their full number until after the thirty-fifth year and even then may appear and disappear with marked irregularity, bearing some relation seemingly to the hemorrhages by being less conspicuous if a considerable interval has elapsed between them. The bleeding varies greatly in frequency and severity, death resulting in some cases from the amount of blood lost. The hemorrhages are usually the result of traumatism except the bleeding from the nose which is spontaneous in its onset. Anemia, vertigo, headache, weakness, dyspnea on exertion, palpitation and swelling of the ankles have also been noted in this affection as a result of the hemorrhages. The outlook is not encouraging, as the hemorrhages are prone to increase in severity as middle life is approached.

The *treatment* is unsatisfactory, as the bleeding is often checked with

difficulty. Haynes employed with success local treatment with a bead of chromic acid fused on a probe and says its caustic action may at any time be checked by the application of an alkali. Cauterization of the troublesome bleeding areas produces the most promising results, although not always successful, and the use of radium for the nodular telangiectasias is to be recommended. For the treatment of the anemia iron and arsenic are indicated.

REFERENCES

Raynaud's Disease

Buerger. Circulatory Disturbances of the Extremities. W. B. Saunders & Co., 1924.
Cassirer. Die Vasomotorisch-tropischen Neuroses, Berlin, 1912.

Erythromelalgia

Cassirer. Die Vasomotorisch-tropischen Neuroses, Berlin, 1912.

Scleroderma

Lewin and Heller. Die Sklerodermie, Berlin, 1895.

Pathological Obesity

Dercum. Univ. Med. Mag., i, 140-150, 1888-1889.
Lyon. Arch. Int. Med., vi, 28-120, 1919.

Progressive Lipodystrophy

Parkes-Webber. Lipodystrophia Progressiva, London, 1918.
Smith, H. L. Johns Hopkins Hosp. Bull., xxxii, 344-350, 1921.

Milroy's Disease

Hope and French. Quart. Journ. Med., i, 312-329, 1908.
Milroy. N. Y. Med. Journ., lvi, 505-508, 1892.

Trophedema

Cassirer. Die Vasomotorisch-tropischen Neuroses, Berlin, 1912.

Hereditary Hemorrhagic Telangiectasia

Steiner. Arch. Int. Med., xix, 194-219, 1917.

METABOLIC DISEASES

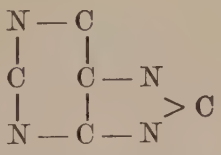
CHAPTER XX

GOUT

JOSEPH H. PRATT

Definition.—Gout (podagra) is a disease of the joints associated with an inborn disturbance of the uric acid metabolism, which results in an increase of uric acid in the blood and a diminished excretion of uric acid in the urine. It is characterized clinically by recurring attacks of arthritis, associated with the deposition of sodium urate in and about the affected joints.

Origin of Uric Acid.—The source of uric acid is a complex substance, nucleic acid, which is found in the cell nuclei of all animals and plants. Nucleic acid contains substances called purin bases which are its most characteristic constituents. The word purin is derived from *purum uricum*. The purin framework or nucleus is composed of five atoms of carbon and four of nitrogen.



The simplest member of the series is the hydrogen compound, purin ($C_5H_4N_4$), which is not found free in nature.

The addition of oxygen to purin results in the formation of hypoxanthin, xanthin, or uric acid, according to whether one, two or three atoms of oxygen are added. Uric acid is therefore tri-oxypurin.

If an atom of hydrogen in purin is replaced by an amino group (NH_2), then adenin (aminopurin) is formed. The addition to this of one atom of oxygen gives rise to guanin, which is amino-oxypurin. The nucleic acid of the cell nucleus contains only the two purins adenin and guanin. They are present in equal amount. By the addition of methyl groups to purin the important methylpurins are formed—theobromin, theophyllin, and caffein.

Protein does not contain purin and hence uric acid is never a product of protein metabolism as was formerly taught. The formation of uric acid from nucleic acid can be shown experimentally by digesting ox spleen which is rich in nucleic acid in the form of nucleoproteins. If this spleen pulp is well supplied with oxygen, uric acid is formed. If no air is conducted through the mixture xanthin and hypoxanthin are produced. After feeding foods rich in nucleic acid, such as thymus, the uric acid output in the urine is greatly increased. This has been generally regarded as additional evidence of the formation of uric acid from nucleic acid. In light of recent investigations, however, it is doubtful whether the uric acid excreted after feeding purins is formed directly from the purins fed.

Sources of Uric Acid in the Urine.—It is generally held that the uric acid in the urine comes in part from the tissues of the body and in part from purin substances contained in the food. The former is called endogenous uric acid, the latter exogenous uric acid. When a person is on a purin-free diet the daily output of uric acid is rarely more than 0.6 gm. or less than 0.3 gm. It was formerly held that the endogenous uric acid was constant for an individual. Some persons do exhibit very slight variations from day to day, but in the majority of subjects examined the variation in uric acid output is considerable. If the caloric value of the purin-free diet is markedly increased or decreased, the uric acid excretion will increase or decrease. If a large amount of protein free from purin is fed, the uric acid output will rise. In a fasting state from twelve to fifteen hours after the last meal the uric acid in the urine falls to a lower level than it does on a purin-free diet. Mareš believes that the uric acid output of a person is constant in the fasting state. After the second day of fasting there is a rise in the uric acid. The excretion of uric acid is less during the night than during the day, and is greatest in the forenoon.

When food rich in nucleic acid is fed, such as thymus or liver, there is a marked rise in the uric acid output. This has been regarded as clear evidence that the nucleic acid in the food, or purin, such as hypoxanthin, when fed is directly converted into uric acid and excreted as such. There are certain weighty objections to this view. (1) No constant percentage of a purin substance contained in the food reappears as purin nitrogen in the urine. It may vary in normal persons from 8 to 74 per cent. (2) Even when very large amounts of purin are fed the uric acid output is rarely more than 1.5 gm. and usually less than 1 gm. The small percentage of purin of food excreted in the urine was formerly explained as due to destruction of the purins by bacteria in the lower part of the intestines. Schittenhelm has shown by experiments that nearly all the nucleic acid of the food is absorbed from the upper part of the intestine. He found very little purin substance in the lower part of the ileum. (3) Proteins, carbohydrates and amino-acids may increase the uric acid output, although

to a smaller extent than purins. (4) Cinchophen may cause a greater increase than a meal rich in purins. (5) Uric acid injected directly into a vein may pass directly into the tissues and hours may elapse before the uric acid output increases. (6) When purin is fed in the form of meat the uric acid excretion rose within an hour while urea excretion did not increase until the third hour (Mareš). The rise in uric acid occurred before the nucleic acid of the food could have been converted into uric acid. (7) Adenin injected into the blood causes a rise in the uric acid output (Schittenhelm, Brugsch), yet as the human tissues cannot convert adenin into uric acid (Jones) it is improbable that the adenin is itself changed into uric acid. (8) Puncture of the sugar center in the dog's brain causes an increased output of allantoin (Brugsch). This experiment suggests that uric acid, like sugar, is stored in the liver and can be readily utilized.

Weighing all the evidence the conclusion seems probable that purins in the food after digestion enter the tissues and either by stimulating some part of the nervous system cause the stored uric acid to be excreted in the urine, or the precursors of uric acid may stimulate cellular activity directly and thus increase nucleic acid catabolism.

Nucleic acid occurs in the form of simple nucleic acid called a mononucleotid and of complex nucleic acid composed of four mononucleotids and called a tetranucleotid. A simple nucleic acid is made up of a molecule of purin or a molecule of pyrimidin united to a molecule of sugar and a molecule of phosphoric acid.

In the cell nucleus of all plants and animals are four simple nucleic acids (mononucleotids) joined together to form a complex nucleotid (tetranucleotid). Adenin and guanin form a part of the complex nucleic acid existing in the nucleus of every cell. This complex nucleic acid is united to a protein molecule forming a substance called nucleoprotein. The protein portion of the nucleoprotein is digested by peptic and tryptic ferments. Then the complex nucleotid freed from protein is split by the secretions of the small intestine into its constituent simple nucleic acids (mononucleotids). These simple nucleic acids according to Tannhauser are readily soluble in water and are probably absorbed from the intestine without further change. If so, the purins adenin and guanin enter the circulation each bound to a molecule of sugar and of phosphoric acid. If the phosphoric acid is split off a compound of purin and sugar is left, to which Levene has given the name of nucleosid. Davis and Benedict have recently isolated from beef blood as a crystalline substance a uric acid nucleosid in which uric acid is joined to a sugar.

A series of ferments converts nucleic acid into uric acid. One ferment changes a nucleotid into a nucleosid by splitting off a molecule of phosphoric acid. Another ferment breaks down the nucleosids, adenosin and guanosin into adenin and guanin by freeing them from the molecule

of sugar to which they are attached. There are also two deaminizing ferments in the body which can convert adenosin and guanosin into hypoxanthin and xanthin without liberating the sugar. The resulting compounds are still nucleosids. Probably these are broken up very quickly into free oxypurins as Thannhauser and Ottenstein found that an extract of human liver converted adenosin and guanosin in a short time into xanthin and uric acid. Adenase, the ferment that changes adenin into hypoxanthin, is not found in any human organ, but a deaminizing ferment is present and by its action the NH_2 molecule in adenin is replaced by a molecule of oxygen, thus converting adenin into hypoxanthin. Xanthin oxydase which changes hypoxanthin and xanthin into uric acid is found only in the liver of man. Uricase, the ferment which converts uric acid into allantoin, is found in all the lower animals, but is absent in man and in the higher apes. In man uric acid is probably the end product of purin metabolism, although definite proof of this has not been discovered.

Etiology of Gout.—Although much is obscure regarding the pathogenesis of gout, certain causative factors are clearly recognized. Heredity plays an important part, especially among the rich. Physical indolence and gluttony favor its development. Probably excessive meat eating is responsible for gout, rather than overindulgence in other articles of food. The disease is certainly rare in southern Europe, where the protein of the diet is largely of vegetable origin, and it is said to be unknown in Japan. Alcohol, especially in the form of porter and heavy wines, is undoubtedly a predisposing factor. Lead favors in some way the development of gout, but is of less importance etiologically than alcohol.

Gout is a disease of mature life. It is much more common in men than in women. In Lindsay's series of 569 English cases, 85 per cent were males and 15 per cent females.

Factors which may excite an attack of gout vary: (1) slight trauma to a susceptible joint; (2) a meal rich in purins, especially when a gouty subject has been living for some time on a purin-free diet; (3) digestive disturbances; (4) indulgence in alcohol; (5) enforced rest;[1] (6) climatic factors seem to have an influence—at least, attacks are more frequent in the spring and fall than at other seasons.

Nature of Gout.—That uric acid is the *materies peccans* in gout is not definitely established, but the weight of evidence favors this theory.

1. Uric acid is deposited in the inflamed tissues during the gouty inflammations, but in no other disease. In the chronic cases deposits of uric acid, sometimes of large size, are found in the ears and about the affected joints. These are called "tophi." On microscopic examination

[1] One of my patients, when put to bed on account of heart failure, promptly developed a severe attack of gout.

they are found to be composed of beautiful acicular crystals of sodium urate.

2. The blood, in gout, usually contains uric acid in larger amounts than in health, both on a mixed diet and one free from purins.

3. The uric acid excretion, in gout, in intervals between attacks, is usually less than in health, both on a mixed diet and on a purin-free diet.

4. There is a retention of uric acid in gout. A day or two before an attack the uric acid secretion reaches its minimum. During the attack there is a great increase in the output. After feeding a meal rich in purins—for example, 200 gm. of sweetbreads—there is in health a marked increase in the uric acid eliminated in the urine in the following forty-eight hours. In gout the excess of uric acid excreted after this meal is less than in health, and the period of increased excretion is delayed, often extending over three or four days. When uric acid (0.5 to 1 gm.) is introduced into a vein it causes usually in gout a much smaller increase in the uric acid excretion than in health.

An increased content of uric acid in the blood for twenty-four hours or more after feeding large amounts of nucleoproteins or injecting uric acid intravenously would seem to be characteristic of the disturbed metabolism in gout.

5. The feeding of large amounts of nucleoprotein has been followed by attacks of gout.

Theories Regarding Gout.—Umber believes that the defective excretion of purins in gout is due to an increased affinity of the tissues for uric acid. It has been shown that cartilage normally exhibits a striking avidity for it (Almagra, Brugsch and Citron).

Garrod believed that the retention of uric acid in the body in gout was due to a defect in the kidney. Recent supporters of this view have held that the permeability of the kidney for uric acid in gout was diminished, even when other substances could be excreted freely. MeClure found a definite depression of renal function in 5 cases of gout tested by modern methods. A similar retention of uric acid has been found in chronic alcoholism, in chronic nephritis, and in cases of chronic arthritis, clinically not gout. Parkes and later Minkowski suggested that uric acid in the blood in gout might be in a form not readily excreted. No definite evidence has been found that supports this view. Many regard the disease as a disturbance of purin metabolism with secondary changes in the kidney.

The acidity of the urine in gout is within normal limits. All attempts to ascribe the deposition of urates in the tissues to diminished alkalinity of the blood have come to nothing.

The Occurrence of Gout.—The disease is still more common in England than in any other country, but there is evidence that it has been

steadily decreasing there for seventy-five years or more. Llewellyn, an English authority on gout, writing in 1921, says that in his opinion the incidence of acute gout has lessened during the past twenty years, and the disease has assumed a milder form. Lindsay, a physician at Bath, as late as 1913 analyzed a series of 569 cases of gout. This is one of the largest series of cases ever collected, exceeding even that of the earlier English physician Scudamore who had notes on 522 cases.

In Germany the disease was increasing in the decade preceding the War. Umber, in his consultation and hospital practice in Altona and Charlottenburg, was able, in 1914, to report his observations on no less than 278 cases of gout. Brugsch, in 1913, analyzed statistics based on 180 gouty patients that had been treated in Kraus's Berlin clinic. During the food blockade gout patients remained free from attacks (Kraus, Brugsch), which is conclusive evidence of the value of undernutrition in the treatment of this disease.

In America gout is relatively rare. Only 61 cases were treated in the wards of the Massachusetts General Hospital from 1821 to 1923. Among the records for the first fifty years—1821 to 1871—there are only two cases. In Baltimore it is more frequently seen than in Boston. Futcher states that among 30,871 medical admissions at the Johns Hopkins Hospital there were 92 cases of gout. Williamson in 1920 reported a series of 116 cases of gout admitted to the Cook County Hospital, Chicago, during a period of six years. Tophi in the ears were present in 65 of these patients. These figures indicate that gout is more common in Chicago than in other parts of the United States. The percentage of gout to the total medical admissions was 0.39, while in statistics published from St. Bartholomew's Hospital, London, it was 0.37. If the figures given are correct, then gout is more commonly seen in the Chicago hospital than in the hospital in London, the home of gout!

Symptomatology—*Acute Gout.*—In typical cases the victim is awakened in the middle of the night by a pain in the big toe. The pain increases in intensity until the torture is unbearable. Toward morning there is some relief from the torment. When day dawns the metatarsophalangeal joint is found to be greatly swollen, the overlying skin deep red, tense and shining. The whole joint is exquisitely tender. Throughout the day the symptoms are less intense, but the second night is one of renewed suffering. The fit of gout lasts from twelve hours to fourteen days or more, depending upon its severity. There is moderate fever; the appetite is impaired; the bowels are constipated; the urine is generally scanty and high colored. As the inflammation subsides there is itching and desquamation of the cuticle.

In only 5 per cent of Garrod's cases was the great toe unaffected in the first attack. Next to the ball of the great toe, the ankle is the most

common seat of the affection. The upper extremities are seldom implicated in the earlier attacks.

The interval between the first and second attack may be a year or more. As the disease progresses the attacks tend to become more frequent and to recur at a definite time of the year—usually in the spring and fall.

Chronic Gout.—This usually develops after a patient has had repeated attacks of regular acute gout. The joints become permanently deformed and attacks of acute inflammation occur more frequently but are less severe. The alterations consist of partial or complete ankylosis of the joints, or the formation of sodium urate around the articulations or in other parts of the body. Many articulations may be involved. The most common site of the chalky concretions is the ear, where they may attain the size of a split pea. They are more commonly situated on the hands than on the feet. Distention of the olecranon and prepatellar bursæ with sodium urate is not infrequent. These enlarged, thickened bursæ are of diagnostic significance.

Complications.—Slight albuminuria and cylindruria are common, even in relatively young gouty subjects. Arteriosclerosis is apt to develop at an early age; usually it is associated with a high blood-pressure, hypertrophy of the left ventricle and a beginning chronic interstitial nephritis.

Differential Diagnosis.—Gout is often confused with other forms of acute and chronic arthritis. Many of the cases that I have studied had been regarded as rheumatism. In acute gout the small joints are chiefly affected, especially the big toe; in acute rheumatism the large joints are involved. The redness of the gouty inflammation is more vivid; the pain is more intense in gout, even when the affected part is at rest; the tenderness is greater. Usually only one joint at a time is affected in gout, while many are often simultaneously involved in rheumatism. There is more edema about the inflamed joint in gout and desquamation and itching at the end of an attack—phenomena not seen in rheumatism. Gout is not accompanied by the drenching sweats so characteristic of rheumatic fever. Gout is hereditary; rheumatism is not. Gout is rare before the age of thirty-five; acute rheumatism is rare after this age. In gout there is no tendency to endocarditis; in rheumatism endocarditis is remarkably frequent. Gout is a disease of metabolism. Acute rheumatism is an infectious disease. The uric acid in the blood is increased in gout, but not in rheumatism.

Chronic gout is distinguished from arthritis deformans by:

1. The history of acute characteristic attacks of gout.
2. The presence of tophi. [2]

[2] In every case in which the possibility of gout exists the skin and subcutaneous tissues of the entire body should be carefully examined. Although most commonly situated on the ears and fingers, deposits may occur in the olecranon and prepatellar-

3. The constant increase of uric acid in the blood.
4. The low output of uric acid when on a purin-free diet.

TREATMENT

Diet and regimen are of more importance than drugs in the treatment of gout. Experience has taught that certain things favor the development of gout and that these injurious agents should be rigidly excluded. The value of frugal and temperate living in the prevention of attacks of gout has been recognized from the earliest times. Galen affirmed that those gouty subjects who indulged in eating and drinking could not be cured. Sydenham recognized that remedies were insufficient in chronic gout unless care was taken as to diet. Cullen was fully convinced that any man who acquired early in life the constant habit of physical labor and abstinence from animal food would be saved from gout, even if he inherited a tendency to the disease.

Until the true nature of gout is known it is unlikely that any cure for the disease will be discovered. The ultimate cause of gout, like truth, as Sydenham said, lies at the bottom of a well. The disease is certainly associated in some way with a disturbance in uric acid metabolism. Not only is the excretion of uric acid in the urine diminished but apparently in every acute attack sodium urate is deposited locally in the inflamed tissues. Uric acid appears to be entirely non-toxic and is now known to be a normal constituent of the blood and tissue juices.

As there is an abnormal amount of uric acid in the organism in gout and a tendency to the formation of local deposits of sodium urate, it seems logical to restrict as much as possible the purins in the food in order to lessen the formation of uric acid. For this reason the use of a diet as free as possible from nucleoproteins is advocated. This is the view of all the German authorities. They regard the fact that gouty patients in Germany ceased to have attacks when forced to take a purin-poor diet during the War as proof of the efficacy of this diet in gout. The diets were

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bursæ when absent elsewhere. No nodule can definitely be diagnosed as a tophus until the characteristic needle-shaped crystals of sodium urate have been demonstrated in its contents. Unless tophi are found in a case of chronic arthritis, the evidence of gout is not conclusive and hence a positive diagnosis cannot be made. Radiograms often show small clear round areas in the bones but these are not pathognomonic of gout. In fact the Roentgen ray is of little aid in diagnosis. The diminished excretion of uric acid in gout after a sweetbread meal or after feeding purins in any other form is of slight value in diagnosis as it occurs in many cases of chronic non-gouty arthritis. Furthermore, a delayed excretion of exogenous uric acid, which Brugsch and Schittenhelm claim is characteristic of the disturbed nucleic acid metabolism in gout, has been found by McClure and Pratt to be as common in arthritis deformans as in gout.

not only low in purins but low in calories. It might be urged that it was the undernutritition that caused the freedom from gout rather than the low content of purin in the food. Most English writers advocate a more liberal diet and are opposed to the idea that purins should be excluded as much as possible from the food. Their arguments are not convincing and the Nestor of English physicians, Sir Clifford Allbutt, is in agreement with the leading medical opinion throughout the world when he says that "the guiding scientific principle of the permanent diet of the gouty is to reduce the intake of purin substances." There is no way yet known of diminishing the purin formation in the body, except by giving the patient less purin in his food.

Purins cannot be completely excluded from the diet for any long period, because even common vegetables are not purin-free. Spinach, green peas and beans contain more than other vegetables and their use should be limited. This is not generally recognized and a meat-free diet is often supposed to be purin-free. Those animal foods are most injurious that contain the greatest amount of purin substances. These are the organs rich in cells—thymus (sweetbreads), liver and kidney. The observation has been made repeatedly that an attack of gout may follow a heavy meal of sweetbreads.

The following figures, given by Burian and Schur, show how greatly the purins vary in different foodstuffs:

100	gm.	thymus	contained	0.414	to	0.516	gm.	purin	N.
100	"	pancreas	"	0.133	"	0.18	"	"	"
100	"	fresh beef	"	0.053	"	0.07	"	"	"
100	"	milk	"	0.0004	"	0.0006	"	"	"
100	"	white bread	"	0.01 minimal traces				"	"
100	"	potato	"	0.0005 to 0.0006 gm.				"	"

The effect on the uric acid excretion of eating a large amount of sweetbreads is well shown in the following chart. This patient, who did not have gout, was on a purin-low diet, except for the sweetbread meal. The output of uric acid rose to the unusually high figure of 1.72 gm. which was eight times the average excretion during the three days preceding the feeding of thymus. It should also be noted that there was a delay of forty-eight hours in the marked use of the uric acid excretion resulting from the meal. Brugsch and Schittenhelm maintain that this delayed excretion is characteristic of gout. McClure and I showed it occurred with equal frequency in arthritis deformans. This subject was a neurotic woman of middle age who aside from acroparesthesia was in good health.

Roasted or broiled meat increases the uric acid output more than boiled meat, for the purins are extracted by boiling. Caviar is free from

purin. Haddock roe, fed to one of my patients, was followed by a marked increase in the uric acid in the urine. Oysters contain purin. Nearly all cream soups, containing a meat stock, are rich in purins. Such soups as well as bouillon which is, of course, pure meat stock should be forbidden.

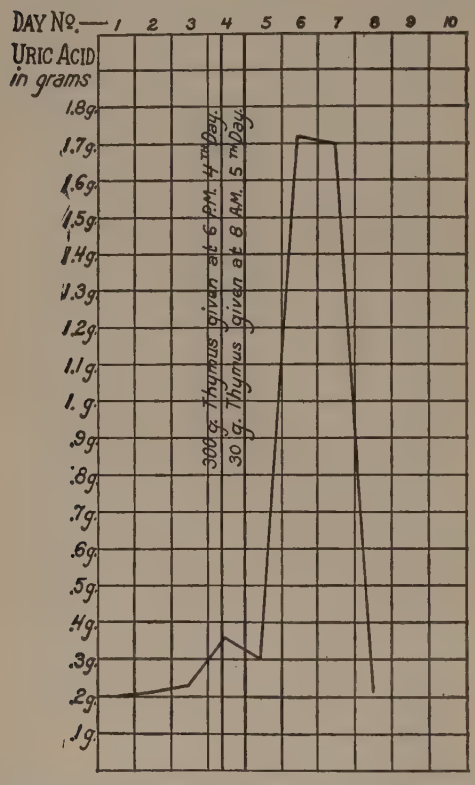

FIG. 1.—THE EFFECT ON URIC ACID EXCRETION OF FEEDING A SWEETBREAD MEAL TO A NORMAL PERSON.

There is no clear indication that proteins deficient in purins should be reduced. I have given my patients an unlimited amount of milk and cheese and have not restricted the amount of vegetable proteins.

Fat and carbohydrates should be given freely, unless obesity or diabetes complicates the gout. All kinds of fresh fruits may be eaten. The use of carbohydrates in gout has been too largely restricted in the past, owing to the teachings of a former generation, but without warrant on either clinical or experimental grounds. If the patients are poorly nourished, they should be given a diet rich in fats and carbohydrates. Even sweets are allowable.

Alcohol should be forbidden. Uric acid is not formed from it, but the nuclein metabolism is disturbed by its use. On a purin-free diet the administration of alcohol is said by von Noorden to be followed by an increase in the uric acid output. Pollak showed that in chronic alcoholics the excretion of "exogenous" purin was diminished and retarded.

Coffee and tea contain methyl-purins but it is doubtful if these are demethylized and converted into uric acid in the body. As coffee can produce a rise in the uric acid output, it is advisable to use coffee that has been freed from caffein; although it is probable that the increased excretion of uric acid is due to mobilization of uric acid stored in the tissues and organs of the body.

The patient should not abandon the purin-low diet, even if no improvement is noted, for many weeks. The change from the ordinary diet to the restricted one may be followed by an attack of gout.

After the patient has been on a purin-free diet for from three months to a year after an attack of gout the experiment may be allowed of giving meat once or twice a week at the midday meal. Any kind of red or white meat or fish may be chosen. The portion, if broiled or roasted, should not weigh over 100 gm. If boiled meat is selected, 150 gm. may be taken. Thymus, kidney, liver, herrings and sardines should be forbidden, as they are very rich in purins. Later the number of purin days per week may be slowly increased.

Purin-poor Diet for Patients with Gout

Breakfast: Fresh fruit. Caffein-free coffee with cream or cocoa. Cereals with cream. One or two eggs. Bacon. Toast or rolls.

Dinner: Vegetable or cream soups, prepared without meat stock. Meat substitutes made with cheese, such as cheese soufflé and Welsh rarebit (Edam, Swiss and Roquefort cheeses contain less purin than American or cream cheese). Macaroni. Rice, potatoes, stewed corn, tomatoes, cauliflower, asparagus, carrots, parsnips, turnips, squash, onions, radishes, celery. Vegetable salads of all kinds; vinegar or lemon juice may be used. White bread or corn bread. Fresh or preserved fruits. Puddings made of rice, sago, tapioca, with cream or fruits sauces. Ice cream. Nuts. Milk.

Supper: Eggs. Rice or hominy. Buckwheat cakes with maple syrup. Salads. Crackers and cheese. Fresh or preserved fruits. Custards. White bread or toast. Milk or weak tea.

The evening meal should be simpler than that taken at midday. Butter should be taken freely at each meal. During the day and evening at least 1½ liters of water should be taken, either plain, aërated, or flavored with fruit juices. The importance of drinking a large amount of fluid should be emphasized. Umber states that observations made in his clinic showed a larger excretion of uric acid in gouty patients when water was given with a meal rich in purins than when it was withheld.

Drugs in the Treatment of Gout

Colchicum.—This medicine has been extolled in the treatment of gout for generations. By some of the wisest and most experienced physicians it has been regarded as a specific in gout. Garrod asserted that sometimes gouty inflammations could be diagnosed by the striking benefit obtained from this drug. One of his patients who suffered from severe attacks said that two or three hours after taking a 2-dram dose of colchicum he felt himself in Paradise. As Thomas Watson says, "a patient may be in helpless agony with a tumefied red hot joint to-day and walking about, quite well, to-morrow."

According to Scudamore the publications of a Mr. Ward called the attention of physicians to the importance of colchicum in gout. Colchicum autumnale, or meadow saffron, was introduced as a medicine by Baron Störk in 1763. Another species of colchicum was employed by the ancients under the name "hermodactyl" and was held in great repute.

In this country the great value of colchicum in relieving the pain and inflammation of gout does not seem to be sufficiently recognized, and I think doses which are too small are often prescribed. A gouty patient of mine, whose father and grandfather had likewise been victims of this disease and had taken colchicum with benefit, told me that even after he had suggested the use of this drug to his physicians they did not employ it.

The best form of administering the drug is the alkaloid colchicin. I have employed Merck's preparation made into pills or tablets containing 1 mg. each. Four to six pills are given a day, usually at intervals of two hours. At the onset of a severe attack four doses may be given within two hours. The drug should then be withheld for twenty-four hours. If diarrhea develops, its use should be discontinued for one or two days.

The wine of colchicum is much used. The dose is 1 to 2 c.c. three times a day for two or three days. It is a good plan to give a larger initial dose (2 to 4 c.c.) and follow this with doses of 1 c.c. Caution must be exercised if the patient has never taken the drug previously, as some persons are so sensitive that the ordinary dose may produce nausea, vomiting, or purging. Different preparations of colchicum that I have used have seemed weak, because in large doses they failed to produce diarrhea.

The mode of action of colchicum is unknown, but is possibly due to an increase of the circulation through the inflamed joints as recent experimental work would indicate. Purgation is not necessary in order to obtain its beneficial effect and should be avoided. Colchicum does not diminish the uric acid in the blood or cause an increased excretion of uric acid by the kidneys, and it tends to diminish rather than to increase the quantity of urine.

The toxic symptoms due to colchicum are vomiting, diarrhea, weak heart action, coldness of the extremities and great prostration.

Cinchophen (Atophan).—In 1908 Nicolaier and Dohrn discovered that the output of uric acid could be markedly increased by the action of several quinolin compounds, especially 2-phenyl-quinolin-4-carboxylic acid, later known as atophan. The excretion of "endogenous" uric acid may be increased 100 to 200 per cent. With continued administration the increased elimination is at an end in two days. It usually exerts its maximum effect in one day. The increase in the uric acid excretion may be pronounced thirty minutes after the drug is taken.

Folin and Lyman were the first to observe that the increased output of uric acid is associated with a decrease in the blood. McLester noted a drop of 50 per cent in the uric acid of the blood three hours after the administration of 3 gm. of atophan. After the drug is discontinued there is a marked fall in the output of uric acid. McLester showed that this drop is accompanied by an increase in the blood. The original level in most cases is attained in two days (Fine, Chace and Bailey).

In chronic interstitial nephritis cinchophen is said to produce little or no increase in the uric acid output (Fine and Chace). This is not true in all cases. In an advanced case studied with Grabfield we found that cinchophen caused a striking rise in the uric acid excretion. The view seems generally held that in gout and in all other conditions except nephritis cinchophen produces a marked increase in the uric acid output. In the spring of 1918 Griesbach and Samson working in Germany gave cinchophen to subjects without any increased output of uric acid resulting. The food shortage was acute at the time and they concluded that cinchophen causes an excretion of stored uric acid and in their subjects, owing to undernourishment, the normal deposits of uric acid were not present. During the past year Grabfield and I have given cinchophen in large doses to eleven well-nourished non-gouty persons with normal renal function and failed to obtain in four any increase in the uric acid excretion.

Cinchophen (1) stimulates the kidneys to excrete more uric acid; (2) sets free stored uric acid; and (3) inhibits purin metabolism.

In gout cinchophen frequently causes a greater elimination of uric acid than in health. In young normal subjects Haskins found the rise above the endogenous level averaged more than 200 mg. during the first twenty-four hours. In a case of gout studied by Folin and Lyman it amounted to 520 mg. In a few cases of gout no rise has occurred. While in health the increased elimination usually ceases within forty-eight hours in spite of the continued administration of the drug, it may persist for a long time in gout. It is important to determine the uric acid output in the urine in cases of gout while cinchophen is given and to continue the drug until the uric acid falls to the endogenous level.

The rapidity with which cinchophen often checks the pain and inflammation in an attack of acute gout is remarkable; one cannot say, however, that it is more efficacious than colchicin. I give 3 gm. of cinchophen a day for three days. If the uric acid output is still high the drug should be continued until the uric acid falls to the previous level. It is conveniently supplied in half gram tablets, one of which is given every two hours with a glass of water.

Cinchophen not only relieves the pain in gout and increases the uric acid elimination but tophi have been seen to diminish under its long-continued administration.

Occasionally an idiosyncrasy against cinchophen has been observed. The symptoms are diarrhea, vomiting, urticaria, headache and tinnitus.

In some cases of gout associated with renal calculus severe colic has resulted from the administration of cinchophen. If this complication is suspected, sodium bicarbonate should be given simultaneously with the cinchophen in sufficient amount to render the urine alkaline.

Cinchophen has frequently been used with success in the treatment of rheumatic fever, and for the relief of pain in chronic non-gouty arthritis. It follows from this that its action cannot be employed as a therapeutic test in the diagnosis of gout.

Neocinchophen.—This is a tasteless substitute for cinchophen, which is said not to disturb the digestion. It is given in the same dosage as the original preparation.

Salicylates.—Salicylates are inferior to colchicum and cinchophen in relieving the pains of gout. Large doses are usually necessary—4 to 6 gm. a day of sodium salicylate. It has long been known that salicylates increase the output of uric acid, and it has been more recently shown that, as with cinchophen, this increase is accompanied by a diminution in the amount of uric acid in the blood.

Hydrochloric Acid.—Vegetables are rich in cations and when a patient is on the prescribed purin-poor diet there exists the possibility of an excess of alkali sufficient to exert injury. Fruits likewise tend to increase the alkalinity of the urine. Hence it is well to give dilute hydrochloric acid (1 to 2 c.c.) daily to patients who are taking diets largely composed of vegetables and fruit. Tophi have been produced in rabbits by injecting uric acid suspended in water under the skin. The introduction of HCl per os hindered the deposit of urates. Pfeiffer injected uric acid subcutaneously in men and found that the inflammatory action was lessened when large doses of acid were taken, while the administration of alkalis increased the local inflammation.

Alkalis.—There is no evidence that alkalis are beneficial in the treatment of gout. Although they have been extensively used for many years, experience has failed to show their value. Sir William Roberts used alkalis in many cases in sufficient doses to keep the urine persistently alkaline, but the gouty attacks were not diminished.

It was formerly held that the administration of alkalis favored the solubility of uric acid in the body and aided its secretion. It was later shown that uric acid probably exists in the body fluids as sodium urate. The addition of sodium ions to solutions of sodium urate decreases the solubility of sodium urate. Van Loghems found in experimental studies that the deposition of sodium urate was favored by the feeding of alkalis.

Mineral Waters.—Mineral waters have been extensively employed. They all contain one beneficial agent which should be taken in large amount—that is, water itself. But there are exceptions even to this

statement. The free use of water in gout complicated by cardiac weakness and edema may lead to serious consequences. Garrod's warning that, in some cases, the action of mineral waters is very injurious should not be forgotten. According to Osler, much of the humbuggery of the profession still lingers about mineral waters—more particularly about the so-called lithia waters.

The value placed on mineral waters varies with the theories held at different times regarding the disturbed metabolism in gout. Clinical experience is still the best guide, and this teaches that spa treatment exerts a favorable influence on the disease. This may be due less to the mineral constituents of the springs than to the beneficial effect of the water itself when taken in large quantity, the regulated manner of life, the change of air and scene, the pleasant surroundings, the simple enjoyments in the open air and the removal of worry and care.

Mineral waters used in the treatment of gout may be classified in five groups as follows: (1) the simple waters, or waters comparatively free from sodium salts (to this group belong Strathpepper, Scotland; Contreville, France; and Buxton, England); (2) the simple alkaline waters (Vichy, France; Neuenahr, Germany; Bedford, Pennsylvania; and Saratoga, New York); (3) the alkaline sulphated waters (Carlsbad, Bohemia; Marienbad, Bohemia; Bedford, Pennsylvania; Greenbrier and White Sulphur, West Virginia; and Richfield Springs, New York); (4) the common salt or muriated waters (Hamburg and Wiesbaden, Germany); (5) the sulphur waters (Harrogate, England; and Aix-les-Bains, France).

The simple alkaline and the alkaline sulphated waters are the ones chiefly recommended for gout. According to Foster the American springs best suited to gouty patients are Hot Springs, Ark., Hot Springs, Va., the White Sulphur Springs, W. Va., and Bedford, Va.

The Uric Acid Solvents.—The uric acid solvents are valueless in the treatment of gout. The list of vaunted remedies of this class includes piperazin, lysidin, lycetol, and lithium salts. One of the few mistakes made by Garrod was the introduction of lithium for the treatment of gout. Lithium, like other uric acid solvents, increases the solubility of uric acid in a test tube, but not in the human body. The use of these preparations should be condemned, not only because they are worthless, but because they give patients a false sense of security, which frequently results in a neglect of the essential dietetic measures.

Physical Therapeutics

Exercise.—Experience has clearly shown the value of physical exercise in the treatment of gout, although physiological studies have failed to explain this beneficial action. The uric acid output is not regularly increased; in fact, it may be decreased by exercise.

At the onset of a mild attack the patient should be permitted to keep up and about, if there is no fever. Regular exercise should be taken in the intervals between attacks. Walking, riding, swimming, golf, snowshoeing, mountain climbing and gardening can all be recommended.

In chronic gout harm may result if patients with eroded joints are compelled to exercise them. In severe cases exercise should not be prescribed until radiograms of the affected joints have been examined.

Hydrotherapy and Thermotherapy.—Electric light baths to the entire body from five to fifteen minutes, followed by a hot circular douche or a Scotch douche, are often of benefit in chronic gout. As a rule, cold procedures are not well borne.

Radium Emanations.—The hope raised several years ago by His and his coworkers, that radium emanations would prove to be of great value in the treatment of gout, has not been realized. The claims of Gudzent that uric acid was destroyed or changed into a more soluble form by radium has been disproved. Fine, Chace and Bailey found that the uric acid in the blood was not decreased when radium was given by inhalations for a long period, in strengths as high as 100 Maché units per liter, nor when administered intravenously in the form of the bromid.

Surgical Treatment

The old view that incision or evacuation of tophi was followed by obstinate ulceration is not borne out by modern experience (Llewellyn). Lindsay found that healing occurs readily provided the incision is made over the more healthy skin towards the base of the swelling. It is far better to open fluctuating tophi than to allow them to evacuate their contents spontaneously, for then suppuration is apt to ensue and the sores remain open a long time. Llewellyn in his recent book (1921) says that in a search of the literature he found only two instances in which operation had been undertaken for removal of gouty deposits in relation to tendon sheaths, bursæ and skin. These were reported by Alexis Thomson. A number of large tophi were removed from both patients. The results were entirely satisfactory. In an unreported case which I studied with Dr. Mark J. Rogers of Boston, he operated twice and removed large discharging tophi from the feet. Although the bones were involved in the gouty deposits the wounds healed readily and the patient was able to walk with less discomfort.

Treatment of an Acute Attack

At the onset of a fit of gout or of premonitory symptoms colchicin or atophan should be given. In my experience both drugs given in large doses, have quickly relieved the pain and inflammation. The mode of

administration has already been described. As the pain is often agonizing, and can be relieved so readily by opium, its use would be advisable unless weighty objections exist against the employment of opium or its derivatives in gout. Sydenham, Cullen and Garrod were agreed that the untoward after-effects of opium in acute gout were so marked that its use was not warranted. Their arguments are not convincing, and the action of opium in gout needs to be studied anew.

The affected joint should be slightly elevated, wrapped in dry cotton wool covered with oiled silk, and lightly bandaged. The joint surface is thus kept warm and moist, and moisture is important as dry heat seems to increase the pain. The dressing soon becomes wet. It should be changed two or three times in the twenty-four hours. In the majority of cases no other local application is needed. If the pain be unusually severe hot fomentations may be used. Anodyne preparations that may be tried are laudanum and water mixed in varying proportions, belladonna liniment, and lead water. Cold applications are usually poorly borne and their use is deprecated.

The diet should be limited to purin-free foods that are readily digested: Toast, oatmeal porridge, boiled rice, cream of wheat, mashed potatoes, apple sauce, simple puddings with fruit sauces; milk, tea or caffein-free coffee with milk. Water should be given freely. If the bowels are constipated, a saline purge may be taken. Magnesium sulphate is preferable to salts containing sodium. After the acute symptoms have subsided the bowels should be regulated by laxative foods.

The patient should be encouraged to leave his bed when the inflammation abates and to walk about, as soon as he can, with the aid of a crutch or cane. The stiffened and swollen joints should be massaged and gently exercised as soon as convalescence is established.

CHAPTER XXI

ARTHRITIS DEFORMANS

FRANK BILLINGS

The writer believes that the great majority of chronic joint diseases are primarily infectious. Of course the clinician will recognize the neuropathic type (Charcot joint); the static type (pes planus, sacro-iliac and lumbosacral maladies); toxic metabolic type (gout); traumatic arthritis and types of senile arthritis as non-infectious. But these non-infectious morbid joints may become infected, because of the lowered resistance of the joint tissues.

The classification of chronic arthritis based upon anatomical and clinical conditions adds confusion to the subject. In the same patient one may observe febrile and non-febrile stages; proliferative and degenerative types of joints; periarthritis, synovitis, ostearthritis and panarthritis, and joints with and without deformities. These clinical and anatomical varieties serve the purpose of clinical description, but do not indicate different diseases in an etiologic sense. Probably variations of type, degree of virulence and dosage of the infectious agents on the one side and the condition of the host as to age, debility due to physical and mental exhaustion from any cause, and other factors determine the clinical and anatomical types. Still's disease may be looked upon as a precocious arthritis deformans, and yet a typical adult form of Still's disease occurs. Malum coxæ senile, a senile monarticular ostearthritis, usually may occur in middle adult life from an infectious source. Rheumatoid arthritis of Garrod, villous arthritis of Goldthwait, and other types are, in my opinion, only varying forms of infectious arthritis and are at best only synonyms of other clinical and anatomical types.

I shall consider in this chapter arthritis deformans of the infectious type. Investigation has shown that strains of streptococci, gonococci, tubercle bacilli, typhoid bacilli and spirochæta pallida are the most common infectious causes of chronic arthritis. When other bacteria are found in the infected tissues of chronic arthritis and myositis they may have etiologic relations to the condition, but are probably present in the tissues as a mixed infection, or purely as parasites. The deformities which occur

in chronic arthritis due to these infectious agents do not differ essentially because the morbid anatomical changes which are produced in the chronic type of infection due to the streptococcus and the gonococcus are essentially the same. The mode of infection is hematogenous and usually from a focal infection. The obstruction due to endothelial proliferation or embolism in the small arteries due to the hematogenous mode of infection is practically the same. In chronic infectious arthritis the virulence of the invading organisms is not high; consequently the tissue reactions excited by the organisms are much less than in the more virulent type, especially of the streptococcus and gonococcus. Therefore, instead of the production of a positive chemotaxis with purulent exudates at the point of infection, as with local infections due to the Streptococcus pyogenes and virulent types of gonococcus, there is in these chronic conditions a tendency to fibrinoplastic exudates in the infected tissues and an attempt to wall off an area of infection. The low virulency of the organism, the embolic mode of infection of the tissues, the resulting tissue reaction, all tend to lessen the blood supply of the infected tissue, through the partial obliteration and destruction of small blood-vessels. In consequence there is a lessened blood supply and oxygenation of the tissues which results in marked malnutrition. Malnutrition leads to secondary metabolic changes in all joint structures, tendons and muscles. These changes have been well described by Nichols and Richardson as both proliferative or hypertrophic and degenerative or atrophic arthritis. Because of these morbid changes, deformities result from muscular contraction and from the changes which occur in the bones and cartilage and other structures entering into the joints. Present knowledge is in accord with Nichols and Richardson that morbid changes both proliferative and degenerative of joint tissue cannot be differentiated etiologically.

If one considers that the infection of joint tissue is hematogenous and that a sufficient dose of infectious organisms in the blood-stream may reach the periarticular tissue or deeper tissue of the joint—that is, the end arteries in the subserous tissues—or through the nutrient arteries involve the medulla of the epiphysis, one may harmonize the morbid anatomical changes which have been so clearly described by Nichols and Richardson.

The reaction set up in the tissues of the external joint structures, in the subcapsular region and in the medulla of the bone, will depend in all probability upon the virulence of the infectious microörganisms and upon the resistance of the general body structures and of the joint tissues. They may be either proliferative with relatively virulent bacteria—especially in young or normal individuals—and necessarily the reaction will be less, or more degenerative in kind in the joint tissues of individuals which are poor because of age, trauma and other conditions which lessen the vitality of tissue. Continued doses of infection from the focus would necessarily

add to the changes described in the joint tissue. The repeated hematogenous infection destroys more blood-vessels, again and again traumatizes the infected tissue and continuously lessens the oxygen supply. We now know that in chronic arthritis infectious organisms, whether streptococci or gonococci, have a relatively low virulence. Of course the degree of virulence varies and consequently the proliferative and degenerative changes especially vary in different individuals. With continued infection of the tissues malnutrition necessarily increases for the reasons named, and this necessarily leads to retrograde metabolism. Whether the retrograde metabolism is due solely to the malnutrition, or whether it is also due in part to irritants in the tissues of bacterial or biochemic origin, does not in any way alter the principles outlined. Therefore, the proper understanding of chronic infectious arthritis involves an understanding of the following principles:

1. The infection of the joints, muscles and other involved tissues with pathogenic organisms which usually are members of the streptococcus group and the gonococcus which are of relatively low virulence; (2) a hematogenous infection with vascular endothelial proliferation and embolism with resulting injury of blood-vessels and small hemorrhages into the infected tissues; (3) lessened blood supply, poor oxygenation, consequent relative starvation of the infected tissues dependent upon the malnutrition and poor oxygenation, all of which are favorable conditions for the continued life and multiplication of the infectious organisms; and finally (4) retrograde metabolism due to the malnutrition and probably to toxins.

In the chronic infection due to the streptococcus, chronic arthritis may occur alone or associated with chronic myositis, and chronic myositis may also occur alone, involving single or groups of muscles. In chronic gonococcus arthritis the muscles are rarely, if ever, involved. Tenovaginitis is, however, more apt to occur in chronic gonococcus infection.

Various anatomical types of chronic infectious arthritis may occur, which doubtless depends upon the degree of bacteriemia, the degree of virulence of the infectious organisms, the resistance of the tissues and the fact that the mode of infection is hematogenous; consequently there may be a periarthritis, a synovitis, an ostearthritis or a panarthritis. Any or all of these types may exist in the same individual. The primary infection may be severe enough to simulate acute rheumatic fever or mild rheumatic fever. Usually the disease begins insidiously, but there may be in many patients periods of increase in temperature usually of a febrile type. There is always a great deal of soreness of the infected tissues, which is aggravated by anything which disturbs the general or local circulation, as chilling the body, fatigue and general nervous irritability. Because of the varying degrees of activity of the focus there may be reinfection from time to time of the joints, muscles and other tissues, with

consequent aggravation of the symptoms. Usually there is but little pain excepting with exercise of the involved organs. Chronic gonorrheal arthritis is more apt to involve the intervertebral joints and ligaments, the sacro-iliac, sternoclavicular and temporomaxillary joints than the streptococcus, but inasmuch as the streptococcus may also infect the four named joints, involvement of them does not necessarily indicate a gonococcus infection. Chronic infectious myositis, which may occur as a part of the chronic streptococcus arthritis, or alone, is associated with shortening of the muscle bundles due to the embolic infection, with subsequent hemorrhage and connective tissue proliferation. At the time of infection there is usually tenderness and pain when an attempt is made to contract the muscles. When at rest there is usually no discomfort. Apparently there is an elective affinity of the infectious organism for certain muscles, notably the masseters, the biceps humeris, the hamstrings, the anterior tibial and erector spinæ muscles. Other muscles are sometimes involved and in some instances practically all skeletal muscles are included in the infection. In all of these chronic types of arthritis and myositis there may be general debility with anemia, emaciation and nervous irritability due to the long-continued infection. Often these general conditions are aggravated by methods of treatment, by starvation diets and purges which weaken the patient, and by the overuse of drugs. In recent years the irrational use of vaccines and of toxic extracts of bacteria has added to the miserable condition of the patients.

These general weakening influences add to the conditions which promote retrograde metabolism in the infected tissues, so that in all patients who present the worst type of the condition there is a tendency to such a degree of retrograde metabolism that the connective tissue group comprising aponeurosis, tendons and cartilage is changed partially or wholly into bone.

TREATMENT

In the treatment the primary necessity is to obtain a knowledge of the patient's general condition and to locate existing foci of infection. The result of rational management will depend partly, in any event, upon the degree and character of the morbid tissue changes in the joints and muscles, upon the command one may have in the management and upon the age of the patient. Destructive lesions of bones and cartilage, bony ankylosis, extensive sclerotic changes and atrophy of muscles cannot be repaired. Indeed because of the destruction of blood-vessels and the resulting want of nutrition, continued retrograde metabolism favors the change of the connective tissue group, tendons, aponeurosis, ligament and cartilage into bone. This is true of all types of chronic infectious nonpurulent arthritis of whatever bacterial type. Therefore, if the treatment

is to result in the arrest of the disease with advanced morbid anatomical changes or in the recovery of those with non-destructive morbid tissue changes, institutional care is required to insure the necessary command of the patient over a sufficiently long period of time to remove all focal sources of infection, to build up general nutrition and to restore as nearly as possible the blood circulation in the infected tissues. This method of management is necessary to stop the sources of systemic infection, to build up the body defenses against the existing systemic infection, to improve the general and local nutrition as the chief means of arresting retrograde metabolism and at the same time to promote resolution of the morbid infectious processes. Rationally the younger the patient the readier will be the response to the management.

In the preliminary general management one may need the aid of qualified specialists in the examination of the nasopharynx, ears, accessory sinuses, pelvic organs and blood, and Roentgen films of jaws and plates of joints to locate etiologic infectious foci and to determine the degree of the joint changes. Microscopic examination and cultures of blood, accessible exudates of joints and of foci in the head, pelvis and elsewhere and of the urine and feces may give valuable information of the character of the bacterial infection. With the consent of the patient always, a harmless and, under local anesthesia, painless removal of pieces of infected muscle, joint capsule, fibrous nodes and lymph-nodes proximal to the infected tissues enables one to study the morbid histology and with a proper technic to isolate the causative infectious microörganisms from the tissues. But important as the study of the exudates, tissues and bacteria may be, the real and important principle is to know all that one may of the physical condition of the patient. Following this diagnosis, the management includes:

1. The removal of all primary and, if possible, all secondary foci of infection. To make sure that all sources of focal infection have been obliterated, repeated examination should be made. Buried tonsillar tissue may be left at the primary tonsillectomy. An infected sinus may not have been adequately treated. Alveolar abscess may finally require the extraction of the tooth. An apparently cured gonococcus infection of the prostate and seminal vesicles may recur. Constant vigilance is necessary to insure the abolition of continued systemic reinfection.

2. The building up of the natural defenses of the body. To accomplish this involves close attention to important principles, including mental and physical rest, nourishing food, restorative tonics when indicated, cheerful environment, good air and sunshine and with some patients the use of suitable bacterial antigens as vaccines to stimulate the formation of specific antibodies in the tissues of the patient. Mental and physical rest must be rationally supervised to meet the idiosyncrasies of the individual. Isolation and continuous bed confinement may be exchanged for

open ward and partial chair treatment to meet the viewpoint of the patient and thus promote the most efficient rest of mind and body. This absolute rest must be maintained until in febrile cases all fever shall have disappeared and also until the severe soreness of the joints and muscles aggravated by motion shall have diminished, for until then the exercise of infected tissues lowers the natural resistance and thereby increases the morbid process of the joints and muscles. Often the temporary application of restraining bandages, splints and casts may favor the diminution of the local infection. The usually poor general nutrition of patients with chronic infectious arthritis calls for a generous mixed diet including an abundance of fats, oils, green vegetables and fruits. The emaciated tissues demand a full allowance of protein-containing food, both animal and vegetable. A plentiful amount of water, milk, buttermilk, cream and fruit juices must be taken. As in other debilitating chronic diseases, some of these patients show lowered carbohydrate tolerance. Individualism in diet is therefore necessary. When necessary, hematinic and other tonics and laxatives and simple analgesic palliatives, such as the salicylic acid compounds, may be judiciously given. There are no specific drugs to be used and narcotics should be avoided in these chronic diseases.

The mental depression of this class of patients retards improvement; hence the need of a constant, cheerful environment and an optimistic attitude of all who come in contact with them.

With the sources of systemic infection obliterated, and the existing systemic infection diminished or entirely controlled by the management described, other measures must be added to the treatment which may stop further retrograde metabolism and in favorable conditions may result in the restoration of normal anatomical and functional conditions of the joints and muscles. These measures are so important that the failure to apply them adequately means failure in the whole management. The object of their use is to attempt to restore nutrition to the starved tissues of joints and muscles which have been deprived more or less of blood and oxygen by the embolic mode of repeated infection from the primary focus.

In addition to the measures already advised to increase the general nutrition, the local malnutrition may be wholly or partly overcome by an improvement of the general and local blood circulation. The measures consist of hydrotherapy, active and passive exercise, local application of superheated dry air and the Bier blood congestion method by the application of the rubber bandage.

Hydrotherapy in the form of alternating hot and cold shower or spray baths, applied daily for a few minutes, flushes the blood to all the parts of the body without fatigue to the patient. If the force with which the water strikes the body is relatively high, the improvement of the circulation is greater. The tonic effect upon the circulatory organs of the application of cold water to the skin is well known. A cold plunge bath is dis-

agreeable to these enervated patients. The alternating hot-cold spray repeated several times in a few minutes is borne without complaint, and the result is quite as good as the use of the cold bath alone. In the absence of facilities for applying shower or spray baths, salt glows and alcohol rubs may be utilized as poor substitutes of the cold bath.

Passive exercise of joints and muscles may be given by nurses or more efficiently by individuals trained to give massage. Occupational therapy is helpful in restoring function as well as in diverting an irritable patient. Active calisthenic exercises may be so taught that under proper supervision each patient will have the benefit of periods of exercise modified to meet individual conditions. Other active exercise, like walking, riding, driving, swimming and gymnastic work, may be taken up at the proper time. An individual qualified by education and experience should have the supervision of the treatment by baths and other forms of physiotherapy.

Chronic arthritis due to *syphilis* may be recognized from the history and by Wassermann blood serum test. The proper application of arsphenamin, mercury and the iodids in addition to hygiene and physiotherapy will afford great relief. Spondylitis deformans requires the attention of the orthopedic surgeon in addition to the general management outlined above. *Static* types of arthritis require proper exercises and apparatus to overcome the faulty postures and displacement of organs and bones.

Vaccination in Arthritis.—For a period of years the writer used autogenous vaccines in the treatment of arthritis. The cultures of the bacteria used were made from confined infections about the mouth, throat, nose and other sites. Subcultures were made of dominant colonies of bacteria grown on blood agar and other solid mediums. Monovalent and polyvalent vaccines were made of dominant streptococcus strains. In some instances the vaccines were made from strains isolated from human tissues, after animal passage. Some vaccines were sensitized with antiserum obtained by inoculating a horse with strains of streptococci obtained from the infected tissues of arthritic patients. These autogenous vaccines were used hypodermically every five to seven days in the dose of 100,000,000 to 2,000,000,000 or more. In a few patients daily vaccination was practiced experimentally. The local, focal and general reaction following vaccination was carefully observed. Local reaction in the form of circumscribed redness, elevation of skin and some tenderness usually occurred in the first three or four injections. General reaction evinced by rise of temperature and general body discomfort was practically absent. Focal reaction manifested by objective evidence of disturbance of joint tissues did not occur. Some patients expressed the opinion that the vaccinations were followed by less discomfort, while others complained of more pain. The opsonic index was estimated painstakingly, before and after vaccina-

tion. It was used as nearly as possible as a guide to vaccine dosage and time of revaccination for many patients over a long period of time. Two hundred and twenty-nine patients received vaccines. One hundred and sixty-four received no vaccines. All received the general management outlined above. The result of the management was quite as good in the unvaccinated as in those who received the vaccine.

REFERENCES

Axhausen, G. Uber das Wesen der Arthritis Deformans, Berl. klin. Wchnschr., l, 298, 1913.

Barker, L. F. Differentiation of the Diseases Included under Chronic Arthritis, Am. Journ. Med. Sc., cxlvii, 1, 1914.

Bier, August K. G. Text Book of Hyperemia, 439, 12°, Rebman Co., New York.

Billings, Frank. Chronic Infections and Their Etiologic Relation to Arthritis and Nephritis, Arch. Int. Med., ix, 484, 1912.

——— Chronic Focal Infection as a Causative Factor in Chronic Arthritis, Journ. Am. Med. Ass., lxi, 819, 1913.

——— Clinical Aspect and Medical Management of Arthritis Deformans, Illinois Med. Journ., xxv, 11, 1914.

——— Focal Infection, Lane Medical Lectures, D. Appleton & Co., New York, 1916.

Billings, Frank, Coleman, Geo. H., and Hibbs, William G., Chronic Infectious Arthritis, Statistical Report with End Results, Journ. Am. Med. Ass., lxxviii, 1097, 1922.

Davis, D. J. Bacteriologic and Experimental Observations on Focal Infections, Arch. Int. Med., ix, 505, 1912.

Ely, Leonard W. Diseases of the Bones and Joints, Surgery Publishing Co., New York, 1914.

Garrod, A. E. Rheumatoid Arthritis, System of Medicine, Albutt & Rolleston, London.

Goldthwait, Joel E. Our Present Understanding of the Rheumatoid Diseases, Wisconsin Med. Journ., x, 243, 1911-1912.

Hastings, T. W. Complement-Fixation Tests in Chronic Infective Deforming Arthritis and Arthritis Deformans, Journ. Exper. Med., xx, 52, 1914.

Irons, Ernest E., and Nicoll, H. K. Complement-Fixation in the Diagnosis of Gonococcal Infections, Journ. Infect. Dis., xvi, 303, 1915.

Jackson, Leila. Experimental Streptococcal Arthritis in Rabbits, Ibid., xii, 364, 1913.

Jones, R. L. Arthritis Deformans; Comprising Rheumatoid Arthritis, Osteo-arthritis and Spondylitis Deformans, W. Wood & Co., New York, 1909.

Lovett, R. W. The Causes and Treatment of Chronic Backache, with a Consideration of the Diagnosis of Sacro-Iliac "Relaxation," Journ. Am. Med. Ass., lxii, 1615, 1914.

Marie, P. Sur la spondylose rhizomélique; anatomie pathologique et pathogénic, Nouvo. inconogr. de la Salpêtr., Paris, xix, 32, 1906.

McCrae, T. Typhoid and Paratyphoid Spondylitis, with Bony Changes in the Vertebræ, Am. Journ. Med. Sc., New Series, cxxxii, 878, 1906.

——— Typhoid Spine, Bull. Johns Hopkins Hosp., xxii, 75, 1911.

——— Arthritis Deformans, Modern Medicine, v, 895, Philadelphia and New York, 1915.

Nichols, Edward H., and Richardson, Frank L. Arthritis Deformans, Journ. Med. Research, New Series, xvi, 149, 1909.

Pemberton, R. The Metabolism, Prevention and Successful Treatment of Rheumatoid Arthritis, Am. Journ. Med. Sc., clxvi, 895, 1913; clxvii, 265, 423, 1914.

Rosenow, E. C. Etiology of Arthritis Deformans, Journ. Am. Med. Ass., lxii, 1146, 1914.

CHAPTER XXII

DIABETES MELLITUS

R. T. Woodyatt

CONCEPT OF DIABETES MELLITUS

The Disease.—The distinctive feature of all cases of diabetes mellitus is a certain anomaly of the metabolism. This same metabolic anomaly may be brought about by more than one disease process. It occurs regularly in the disease of obscure pathogenesis which we know as diabetes mellitus of the commoner type. It also occurs in the course of diseases of known pathogenesis affecting the pancreas, as for example in the course of infections that actually involve the pancreas, with all their immediate and remote effects, such as hemorrhage, necrosis, atrophy, fibrosis, stone, and so on. In the latter case when the local disease is diagnosable the tendency is to speak of *pancreas diabetes,* whereas, in the commoner type of case, the tendency is to speak simply of diabetes mellitus without qualification. In both types of cases we are dealing with the same metabolic derangement, but the course and progress of the symptoms may differ very greatly depending on the nature and course of the underlying disease process.

Metabolic Anomaly.—The metabolic anomaly that characterizes all cases of true diabetes mellitus, whether of the commoner "idiopathic" type or whether of the type that has its origin in local infections or other definitely recognizable diseases involving the pancreas (pancreas diabetes), consists essentially in an abnormal lagging or abrupt halting of the power of the body to utilize glucose which manifests itself in a rising excretion of glucose when the glucose supply from all sources (that is, carbohydrate, protein and glycerol of fat, exogenous and endogenous, taken collectively) rises above some limit that is characteristic for the particular case at the time and under the conditions of observation. The meaning of this statement will be made clear in the following paragraphs.

The Glucose Supply in Fasting.—A normal individual who is neither fat nor thin but who has an average distribution of bone, muscle and fat and who weighs 50 kg., if subjected to fasting for several days, will actually produce heat at the rate of about 30 calories per kg. at light occupation, or about 1,500 calories per day. After the first day in which he uses up the major part of his stored glycogen, he will produce this

heat almost wholly from protein and fat. If one examines the data obtained by F. G. Benedict in his calorimetric studies on inanition and fasting, he will find that Benedict's subjects catabolized on the average some 1.5 gm. of protein and 2.5 gm. of fat per kg. day, or more fat than this in the case of more fleshy individuals, and his findings are in harmony with the published results of other investigators. It is simply a restatement of recorded facts to say that a normal individual having an average proportion of fat in the body and weighing 50 kg. will break down some 75 gm. of tissue protein and some 120 to 130 or more gm. of tissue fat per day *at light work.* To this may be added a little carbohydrate (glycogen). If this quantity of protein yielded a weight of glucose corresponding to 58 per cent of the weight of the protein catabolized and if the glycerol of the fat yielded glucose corresponding to 10 per cent of the weight of the fat catabolized, and if the glycogen were negligible, there would be formed in the body 58 per cent of 75 plus 10 per cent of 130 or 56.5 gm. of glucose from endogenous sources in the day. Of course, if the fasting subject is fat when fasting begins, relatively more fat will be burned and less protein; and, if the subject is thin but still well muscled, he may break down relatively less fat and more protein. Again if the individual is emaciated both as to fat and muscle, he will break down less of both fat and protein but relatively more protein and less fat than the individual who has a normal amount of body fat. With these reservations in mind it may be said that fasting in the case of an individual in an average state of nutrition at light work implies a glucose supply per day of about 55 gm. per 50 kg. of body weight. Notwithstanding this, fasting usually results in "desugarization" of the urine in cases of diabetes of even marked severity. Diabetics who pass into the non-diabetic status as a result of fasting are able to burn their endogenous glucose supplies as completely as though they were normal.

Basal Replacement Diets.—This introduces a second consideration of much practical importance to the physician who is treating diabetic cases. If a specified individual in fasting and at light work breaks down 75 gm. of protein and 130 gm. of fat for a total heat production of 1,470 calories and *if he then be given in the form of food the same quantity of fat that he breaks down in fasting, namely, in this instance 130 gm., the feeding of this amount of fat will not materially alter the amount of fat burned.* He will still burn about 130 gm. of fat and still produce about the same number of calories as before. *It may even happen that with the fat feeding he will catabolize less protein than in fasting and so, by receiving food, actually lower his total caloric output, his protein breakdown, and his total endogenous glucose supply.* By the feeding of just the right amount of fat it is commonly possible to lower the protein breakdown to between .5 and .7 gm. per kg. of body weight, or to less than half

of what it may be in fasting. A person *at absolute rest in bed* produces on the average 25 calories per kg. or 1,250 per 50 kg. per day, and as a general rule if a patient is given a diet containing .5 to .7 gm. of protein and 2.0 gm. of fat per kg. of body weight, and if he is kept quietly in bed all may be done that can be done by total fasting and frequently more.

Now, returning to the former theme, a diabetic individual weighing 50 kg. in an average state of nutrition, at rest in bed will produce about 25 calories per kg. day or 1,250 calories. His actual basal metabolic rate may be determined if feasible, but experience will show it to be, as a rule, very close to 25 calories per kg., so that the actual reading of the basal metabolic rate is of real clinical importance in treating diabetic patients only in cases that are markedly above or below the average in nutrition, or in complicated cases. If desired also, one may take the weight and height into consideration and calculate the surface area from the excellent charts of Du Bois, in which case one may estimate the heat production in terms of calories per square meter of surface instead of estimating it from the weight alone, but for practical purposes in the routine care of diabetic patients of average shapes the weight in kilograms times 25 gives a sufficiently close approximation of the probable basal caloric requirement. Let us then give the above patient .5 to .7 gm. of protein and 2.5 gm. of fat per kg. or in all for the 50-kg. person 25 to 35 gm. protein and 125 gm. fat. This will yield 1,225 to 1,265 calories as required. On this diet the patient will receive enough calories and nearly, if not quite, enough protein to maintain him in caloric and nitrogenous equilibrium so long as he remains at rest in bed. Assuming that these conditions are fulfilled, the glucose supply will then be 58 per cent of the protein plus 10 per cent of the fat for a total of 27 to 33 gm. (plus a small amount from glycogen). Practically, in order to construct a palatable diet, it may be desirable to use such an article as cream and this will introduce a little carbohydrate not included above. In that case the glucose equivalent of the food supply may total 50 to 55 gm., just as though the patient were fasting (50-kg. patient, average state of nutrition, rest in bed). *Notwithstanding this glucose supply the urine becomes sugar "free" in all except the most severe cases. Even very severe cases of diabetes burn the 50 gm. of glucose as completely as though they were normal* (atypical mild cases excepted).

Sharply Definable Limits of Tolerance.—Now if we begin with such a diet and every second or third day increase its glucose value by 10 gm. and every day measure the quantity of sugar in the 24-hour urine in mg. by a suitable method for estimating the sugar of normal urine (Benedict-Osterberg, or Folin-Berglund), it will be found in the beginning at 300 to 500 mg. or thereabouts (10 mg. per kg. or less) mostly non-fermentable. As the glucose value (G) of the food supply rises, one of several things

may occur: (1) there may be no change; (2) there may be a temporary rise after each new addition followed on the next day by a restoration of levels; (3) there may be a gradual slight rising tendency. In any case the total excretion remains below 1,000 mg. or 20 mg. per kg. Then at some stage, with or without warning, the excretion begins to rise rapidly. In a severe case the rise may be extremely abrupt with the G at 60 to 70 or 80 gm., a single increment of 10 gm. added to the diet causing the appearance of 5 to 10 gm. of sugar where before there were milligrams and thereafter any further addition may be excreted *in toto*. This may also be followed by a falling of the tolerance below its former level so that the patient then excretes even more than the last increments to the diet. In less severe cases the rising tendency appears only when the glucose supply is higher and then less abruptly, and, after the rising tendency has been noted, further increases may lead to more gradually rising percentage excretions. Thus if the first rising tendency is noted with a supply of 120 gm. of glucose, it may require several subsequent additions to the diet before 100 per cent of the last increment is excreted.

A normal 50-kg. individual seldom excretes more than 10 to 20 mg. of sugar per kg. day, even on diets with glucose values of 400 gm. and upward. In the non-diabetic the utilization rises to keep pace with the supply up to the limit of any supply that can be given by mouth. In the diabetic the same is true up to a certain point, but as the supply rises progressively higher and higher utilization fails to keep pace with the rising supply and suddenly comes to a standstill or progressively lags behind.[1]

Mechanism of Diabetic Anomaly

The anomaly of the metabolism described in the foregoing paragraphs as characteristic of true diabetes mellitus—the abrupt coming to station or progressively lagging power to utilize glucose once a certain limit to the rate of supply has been exceeded—is the expression of a limited power of the body to produce *insulin*, which, thanks to the work of Banting and Best and their colleagues of the Toronto group, is no longer a hypothetical product. Without reviewing their work in detail or that of their predecessors in this field, it may be stated with fair assurance, especially in view of MacLeod's studies on fishes, that in the human body insulin is elaborated chiefly by the pancreatic islets or islands of Langerhans, elsewhere in some degree as shown by Best, but largely by the islets. The failure of the glucose utilization in the diabetic to rise as the supply rises may be conceived as evidence of the failing function of the

[1] These statements are based on partly unpublished observations of several hundred diabetic patients.

insulin producing apparatus. The metabolic anomaly characteristic of the commoner type of diabetes is the expression of a condition of *hypo-isletism*. Other anomalies may of course be associated.

Causes of Hypo-Isletism.—When the pancreas is removed by a surgical operation the cause of an *hypo-isletism* is clear. The same is true in the rare cases of traumatic destruction of the pancreas, a definite example of which is recorded by Wells. When at autopsy in a case of diabetes the pancreas is found in a state of acute inflammation with extensive necrosis, atrophy or atrophy and fibrosis as the result of old infection with or without cysts, stone, etc.; or when in certain cases of advanced arterial sclerosis with mild diabetes one sees the atrophic pancreas largely replaced with fat and fibrous tissue, one does not have far to seek for a cause of hypo-isletism. It is different with many cases of diabetes of the ordinary type, especially those in the young. In such cases, even though during life the degree of diabetes has been very severe, the pancreas may show little or no change when examined by all ordinary methods. In such cases there may be an absence or paucity of islets, the islets may be fibrosed or in a state of hyaline degeneration or of the more questionable "hydropic degeneration." Perhaps all of these represent stages of the same disease. Again none of these changes can be found and the pancreas cannot be distinguished from a normal organ even by the skilled pathologist working with present-day methods. What, then, causes the islets to go out of function without showing visible changes or to degenerate both in function and structure without any local pancreatic disease apart from the islets is an unsolved problem. The writer feels that the symptomatology of ordinary diabetes and the morbid anatomic findings or absence of findings suggest a disease of the sympathetic autonomic nervous system.

Physiological Considerations.—The normal individual liberates in the body more insuline when he receives an increased glucose supply and less when the supply sinks. The regulation of islet function is automatic. A rising glucose supply stimulates the islet nerve-gland apparatus. A falling or low glucose supply permits the apparatus to idle. The clinician may think of this apparatus as he would think of the heart. The healthy islet apparatus may be exercised and hypertrophied. It may be fatigued. It may be rested. If it is imperfect it may be overstrained like a weak heart. Even then, under prolonged rest, it may recover function and go on better for a time. But in ordinary diabetic cases it lacks reserve power and may be broken down by any unusual strain. In all ordinary cases of true diabetes mellitus there is a tendency toward progressive disintegration of islet function. This may be retarded, arrested, rapid or slow, but it tends to reassert itself, especially if when the islet function first shows signs of failure the patient has not passed the noonday of life. The work of the islet apparatus is provided by glucose. Glucose

is its principal whip and burden. Apart from glucose nervous strains, unhappy or stressful emotions, psychic conflicts and bacterial infections are of great significance both directly and indirectly through their power to flood the blood with sugar from glycogen. *To spare a weakened islet apparatus, protect it from overloads of glucose and from stimulating or depressing nerve-born influences of all sorts.*

Acidosis in Diabetes.—The typical acidosis of diabetes consists primarily in the liberation into the cells, blood and urine of unusual quantities of acetone and of aceto-acetic and β-hydroxybutyric acids (acetone bodies). These acids are capable of being excreted in part unneutralized. The remainder is neutralized in the body and this requires bases. One may think of this neutralization as though it were effected chiefly by sodium bicarbonate, to yield the sodium salt of the acid and 1 molecule of CO_2 thus:

(1) H (aceto-acetate) + $NaHCO_3$ → Na (aceto-acetate) + H_2CO_3. H_2CO_3 → H_2O and CO_2, or,

(2) H ((β-hydroxybutyrate) + $NaHCO_3$ → Na (β-hydroxybutyrate) + H_2CO_3, etc.

The sodium aceto-acetate or β-hydroxybutyrate passes out into the urine and the body thus loses some of the base sodium. Other bases besides sodium enter into this process to a lesser degree. A small and variable amount of the diabetic acids may be neutralized in the liver [2] (where they chiefly arise) by ammonium instead of sodium, and this commonly leads to the presence of ammonium aceto-acetate and β-hydroxybutyrate in the urine which cause the total ammonium content of the urine to increase so that when one examines the urine for ammonium in the presence of diabetic acidosis he finds it above the normal (unless indeed this effect is prevented by the administration of *enough* bases stronger than NH_4, such as sodium bicarbonate, in which case the stronger base replaces most of the ammonium).

The acids that play the leading rôle in the typical acidosis of diabetes originate in the fats and protein, but when enough glucose is burning in the body these acids, if formed, do not continue to exist but are themselves oxidized. The occurrence of acidosis of this type is not distinctive of diabetes. The same type of acidosis occurs in fasting or as the result of misbalanced diets, and in fasting, especially in the obese, in pregnancy and in childhood. It is the expression of the burning in the body of a mixture too rich in fatty acids (and the ketogenic amino-acids) and too poor in glucose. The fats are composed of glycerol and long chain fatty acids. When they break down in the body the fatty acids are separated from the glycerol. Each fatty acid molecule when burned is apparently capable of producing one molecule

[2] Based on a study reported by Robert W. Keeton, of the Sprague laboratory, Journ. Biol. Chem., xlix, 411, December, 1921, and earlier literature cited in that article.

of aceto-acetic or β-hydroxybutyric acid. If enough glucose burns with it no aceto-acetic or β-hydroxybutyric acid survives. In like manner proteins are composed of amino-acids. When proteins are broken down in the body amino-acids are liberated. Some of these, like the fatty acid molecules, are capable when burned in the body of yielding one molecule of aceto-acetic or β-hydroxybutyric acid. But if enough glucose burns in the same place and at the same time, these acetone bodies, if formed at all, fail to survive. It would seem that *for the body taken as a whole* one molecule of glucose may have to burn with each molecule of a ketogenic acid in order to prevent the development of an abnormal acetonuria. P. A. Shaffer and Wilder estimate that one molecule of glucose suffices for the complete oxidation of two molecules of ketogenic acid. In any case if one measures the carbohydrate, protein and fat actually being broken down in the body at times when the urine first begins to yield positive qualitative tests for acetone, and if one calculates the quantities of glucose molecules and of ketogenic molecules that could be formed from this carbohydrate protein and fat, it will very often be found, although not invariably, that the ratio of glucose molecules to ketogenic molecules is about 1 : 1. Sometimes acidosis is found when the ratio of ketogenic acids to glucose burning in the body as a whole is lower than 1 : 1. Sometimes the ratio is found higher with no acidosis. The causes of these variations are sometimes clear, sometimes not. But as a general rule *for the body taken as a whole,* the burning of more than one molecule of ketogenic acid to one molecule of glucose will sooner or later lead to acetonuria sufficient at least to detect with the nitroprusside test.

For the physician unaccustomed to think in terms of molecules it may be stated that if an individual is burning 100 gm. of carbohydrate, 100 gm. of protein and 250 gm. of fat it may be calculated that he will form in the body roughly the same number of molecules of glucose and ketogenic acids. In other words *acetonuria is likely to develop when the amount of fat burning in the body equals or exceeds twice the amount of carbohydrate plus half the amount of protein.* Expressing these relations in the form of an equation, when the fat, F, actually burning in the body, equals twice the carbohydrate, C, plus one-half of the protein, P, then acetonuria is likely to develop, that is, when F = twice C + half P. For practical purposes assume that a patient is on a diet that just suffices to maintain him, so that he neither stores in the tissues nor breaks down any carbohydrate, protein or fat of the tissues in excess of the diet. Assume that this diet contains C, 30 gm., P, 40 gm., and F, 100 gm. One wishes to know whether the proportion of fat is high enough to provoke acidosis or not. Twice C is 60, half of P is 20 and 60 plus 20 is 80. The fat of the diet is about 20 gm. high, and acidosis might occur. However the diet is one of low magnitude. If

the patient weighed 50 kg. the total fat would not be more than he would break down from his tissues in fasting at rest. He might show acidosis on the diet but if he burned all of the glucose that it would yield he could not produce *much* acid from the 20 gm. of extra fat, not more in fact than he would produce in fasting. So this diet would probably do no harm in the case of a 50-kg. patient. However, if the patient were a child weighing only 25 kg., the case would be different. The absolute amount of acetone bodies produced would be no less than before but this amount would represent relatively twice the dosage of acids per kg. of body weight and might prove disastrous. *When dealing with diets of magnitudes approximating the basal caloric requirements of the individual, ratios can be ignored, but with diets above basal requirements the danger of too much fat rises with the magnitude,* and in calculating the chances one must not forget that some of the glucose derived from a diet may be excreted unburned. One should be on the lookout with patients receiving more than 25 calories per kilogram when the fat exceeds twice the carbohydrate plus half the protein.

Diagnosis

The diagnosis rests on finding in the urine abnormal quantities of a dextrorotatory fermentable reducing substance (glucose), and in demonstrating that the individual has a definite and characteristic limitation of the power to burn glucose. If one proves in every case of doubtful diabetes that the reducing substance disappears from the urine when fermented with yeast and that it turns the plane of polarized light to the right, he excludes practically all forms of mellituria other than glycosuria. Most cases of persistent glycosuria are truly diabetic, but not all. Even rather marked glycosurias may persist during the latter months of pregnancy without any demonstrable fading of *the power to burn* glucose under a rising supply. The same is true in case of so-called renal glycosuria and there are other confusing glycosurias. Doubtful cases may be placed on a series of graded isocaloric diets having glucose values of 100, 200, 300 gm. respectively and so on upward if necessary. The patient should remain on each diet for at least three days during which the 24-hour outputs of sugar are accurately determined by a method such as that of Benedict and Osterberg or Folin and Berglund. The average excretion for the successive periods may then be plotted. The line or curve so obtained usually gives valuable information. One or more blood-sugar percentage determinations before breakfast when the patient is on each diet may be of assistance if they run persistently low. The true typical diabetic case shows an upward break or bend in the excretion curve beginning at a definite point. *Failing to demonstrate a sharp break or progressive acceleration of the glycosuria*

with a rising glucose supply, one may well hesitate to make too severe a prognosis or impose too rigid restriction on the patient.[3]

Typical cases of diabetes also show a sharp response to insulin. If with an excretion of 5 to 10 gm. of sugar per day 5, 10, or 20 units of insulin given before breakfast fail to desugarize the urine, this is an added suggestion that one is dealing with a mild form of glycosuria that is perhaps not of the same significance as that of the true diabetic. Elderly stout people with advanced arterial disease, have often a mild form of diabetes or glycosuria in which it is difficult to demonstrate by the urine any sharp limitation of the power to burn glucose. In such cases the blood-sugar percentages may run persistently above 0.18 to 0.20 per cent. The entire mechanism is not clear. In some of these cases the changes in both the urinary and blood findings with glucose supplies rising from 50 to 200 or even to 400 gm. may be slight and the response to insulin small. If, in order to keep the urine sugar-free, one must impose on the patient a diet so low that it partly disables him, this and the psychic depression caused by the régime may in some cases work more harm than the disease itself.

Treatment

Hospitalization.—The new case is best treated for a preliminary period in a hospital where the type of disease and its degree and the presence or absence of complications can be determined, where the diet may be balanced, and dependable records obtained for future use. Especially important is the preliminary schooling of the patient or responsible person who subsequently conducts treatment at home under conditions as they are. It is not absolutely necessary that the patient enter a hospital for, if the doctor has the necessary knowledge and takes the time to impart it at home, especially if a nurse can be installed to supervise the diet, the collection of urine and the transport of specimens to the laboratory can all be done at home. But it requires more individual effort and more time, consequently it will not be carried out on the average so well or cheaply at home as in a hospital where the work can be organized. Elaborate hospital facilities, however, are not necessary. One may do excellent work with diabetes with simple equipment. The primary requirement is a good knowledge of the subject. Good history taking, familiarity with clinical symptoms and signs, and sound principles of treatment are more important than blood-sugar and basal metabolic rate determinations.

Diet Kitchen and Quantitative Diets.—A food scales is absolutely necessary. The 500-gm. balance with movable dial, obtainable from Hanson or John Chatillon & Sons, is convenient. It requires but an hour of training to enable any intelligent attendant to measure and tare

[3] Unpublished method.

the household vessels. Place any narrow glass on the scales, add milk or cream to 100 and 200 gm., mark the glass and it is a graduate. A simple ivory or celluloid strip marked as a scale to measure the depth of liquids in vessels and to gauge their diameter or to measure the breadth and thickness of a square of bread or butter can be used in conjunction with the balance and subsequently be carried by the patient when away from home.

Ordering Diets.—Theoretically it is convenient to order diets in terms of carbohydrate, protein and fat, leaving it to the dietitian to make up the menus. Practically the most consistent metabolic results are not obtainable in this way. The dietitian makes up the menus from food tables. Two articles that show the same carbohydrate or protein or fat on the printed lists are to her the same in respect of these things. Actually they are not. On the other hand the particular foods that she uses may run very much the same for considerable periods of time. It is a good practice during the first weeks of a metabolic study when accuracy is the main requirement to order diets by articles in grams and to specify the distribution by meals. One should work with a few staple foods naturally adapted to quantitative work and likely to maintain uniform composition. Eggs weighing 50 gm. can be selected and they vary little in composition. Milk of uniform composition is usually obtainable, also cream with 18 to 20 per cent of fat. If desired, milk samples can be sent to a laboratory for analysis. Even the most difficult cases of diabetes can be well managed if necessary with milk, cream and eggs, plus clear broth, water, tea or coffee. It is not a bad plan in severe cases to begin in this way. In any case all ordinary dietetic work can be done with the foods listed in the following table. It is essentially the same list as that presented on the useful cards devised by Joslin, but the values are here given for 100-gm. instead of 30-gm. portions and the G of each article is added. In making alterations of diets after the period of close observation the use of G simplifies the calculation. The table on page 271 shows the number of grams of carbohydrate, protein and fat contained on the average in 100 gm. of each food (or in one egg weighing 50 gm.) and the number of grams of glucose "G" that may be produced in the body by 100 gm. of each food, or a 50-gm. egg.

Special Diabetic Foods and Food Substitutes.—Formerly certain special diabetic articles were used, such as agar jelly, bran agar and bran gum muffins, "cellu" wafers, mineral oil salad dressings and other non-caloric preparations. They were substitutes for food. It requires the inclusion in a day's ration of only 3 to 5 gm. of gelatin and 45 gm. of bread to make such articles unnecessary. With a case so severe that this cannot be done without inducing glycosuria the diet will be too low for adequate nutrition anyway, and since the advent of insulin it

AVERAGE NUMBER OF GRAMS OF CARBOHYDRATE, PROTEIN AND FAT IN 100 GRAMS OF EACH FOOD

$(G = C + .58\,P + .1\,F)$

Foods	C	P	F	"G"
Vegetables, 5 per cent group	3	1	0	3.6
Fruit, 5 per cent (grapefruit)	5	1	0	5.6
Fruit, 10 per cent	10	1	0	10.6
Gelatin	0	100	0	58.0
Lean meat	0	25	15	16.0
Eggs (50 gm. piece)	0	6	6	4.1
Milk	5	3	4	7.1
Cream, 20 per cent	5	3	20	8.7
Butter	0	0	85	8.5
Bacon	0	15	50	13.7
Olive oil	0	0	100	10.0
White bread	52	9	2	57.4
Oatmeal (dry weight)	67	16	2	76.3
Rice (dry weight)	80	2	0	81.8
Cane sugar	100	0	0	100.0

would seem preferable to allow at least enough food to make substitutes unnecessary and to give the extra 10 to 20 units of insulin that may be required for at least 45 gm. of bread. The use of substitutes, moreover, caters to stomach hunger and patients tend to acquire the habit of using too much of them, with the result that they provoke diarrheas or even serious colitis attacks. In the writer's clinic their use has been discontinued in all but exceptional cases. Other special diabetic foods such as bran-egg-soy bean muffins, casein breads, etc., having some food value and less irritant, are not so objectionable but play no significant rôle in the treatment of diabetes.

Laboratory.—One needs reliable qualitative tests for sugar, acetone, and aceto-acetic acid. Quantitative measurements of the number of grams of sugar in the urine of separate periods is essential for good work with diabetes in general. A method such as that of Benedict and Osterberg or of Folin and Bergelund for the quantitative estimation in milligrams of the sugar in normal urine is also of great practical value both in diagnosis and treatment. In cases of acidosis, estimations of the CO_2 combining power of the blood plasma by the method of Van Slyke give a useful index of the alkali reserve of the body that in some situations should not be dispensed with. Blood-sugar percentage determinations seldom give essential information that cannot be obtained better from quantitative measurements of the urinary sugar, although they add an occasional point. Determinations of the basal metabolic rate are useful especially in intricate cases, but not necessary for good practical work, since the data already obtained make it possible to antici-

pate results with very fair consistency. Determinations of the total urinary nitrogen educate the observer and sometimes reveal unexpected conditions. They are desirable but are not indispensable for good routine work. A formulin titration of the urine for ammonia is many times useful in deciding whether or not a qualitative reaction with ferric chlorid is due to aceto-acetic acid or to some medicine that has been taken. An increased ammonia output strengthens the diagnosis of acidosis and gives an idea of approaching danger. It is done simply in ten minutes. The plasma CO_2 by Van Slyke gives better information.

Guiding Principles in Dietary Management.—Diabetes disables the patient primarily by reducing his power to use glucose with resultant undernutrition and frequently acidosis. Hyperglycemia and glycosuria may at times be disabling with or without undernutrition or acidosis. The objects of treatment are to nourish the patient and to prevent or eliminate acidosis and glycosuria despite the disease. Naturally the object is to accomplish these ends in the highest possible degree for the longest possible time in the highest possible percentage of all cases. As means to these ends one must proceed in accordance with sound principles. The essence of dietetic management is contained in the following precepts:

1. Bring the glucose supply to the tissues from all sources below the limit of the power of the body to utilize glucose with normal completeness, that is, reduce the glucose supply sufficiently to make the urine free of abnormal quantities of glucose. This paves the way for an increasing power to burn glucose on which rests the power to burn fats in the normal manner.

2. Adjust the supply of higher fatty acids (and ketogenic equivalents) in relationship to the quantity of glucose burning in such a way as to make the urine free of abnormal amounts of acetone (and its congeners aceto-acetic and β-hydroxybutyric acids).

3. When the best attainable power to burn glucose is insufficient to permit one to nourish the patient and keep the urine free of abnormal amounts of sugar and acetone bodies, increase the power to burn glucose by the administration of insulin.

For practical clinical purposes the glucose supply may be calculated in grams as 100 per cent of the carbohydrate plus 58 per cent of the weight of the protein plus 10 per cent of the fat actually broken down in the body, thus:

$$(1)\quad G = C + .58\,P + .1\,F$$

In the same sense the supply of higher fatty acids and their equivalents may be estimated in grams as 46 per cent of the weight of the protein plus 90 per cent of the fat actually broken down, thus:

$$(2)\ FA = .46\ P + .9\ F$$

When the ratio of FA: G is 1.5 or thereabouts the balance of ketogenic and antiketogenic materials is near the acetone point in the majority of persons in a fair to average state of nutrition. It will be noted that 46 per cent of the weight of protein or the value given to FA in protein and 58 per cent of the protein weight calculated as G add up to more than 100 per cent. It may therefore be recalled that protein actually contains *no* glucose and *no* higher fatty acids. Protein is made up of amino-acids. But some of these in the body are transformed into glucose after losses and gains of substance. Other amino-acids yield acetone bodies and 100 gm. of protein yields approximately as much acetone bodies *as though* it contained 46 gm. of higher fatty acids. It may also be noted that when a normal person fasts he develops acidosis of the fasting type. A fasting man may excrete 10 to 15 and more grams of acetone bodies in the urine daily. Still he does not go into acid coma. This is because the absolute dosage of acetone bodies is usually not large enough to be dangerous, as previously noted, hence fasting was long used to *control* diabetic acidosis. Still the FA : G in fasting is above 1.5. The same holds true of persons living on basal maintenance diets. But no matter what the FA: G ratio for the diet may be, it will not cause more acidosis than fasting if the diet is no higher in magnitude than the fasting food supply. So when working with diets that contain no more fat than is broken down in fasting one may ignore FA: G. Thus, a *diet* consisting simply of 50 gm. of fat and nothing else would have an FA: G ratio of 45 ÷ 5 or 9.0, but in a man of 50-kg. weight it would add nothing to the acidosis of fasting. Also if the diet consisted simply of 10 gm. of sugar the ratio would be 0 ÷ 10 or 0, still this would have little effect on a fasting acidosis. However when diets rise above basal maintenance levels the significance of the ratio rises in proportion to the magnitudes of the diets. With these facts in mind it will be clear why with a basal maintenance diet the FA: G ratio may be far above 1.5 : 1 without violation of principles.

Detailed Management of a Severe Case.—The following is based on an actual case of *severe diabetes with acidosis but no symptoms of acid poisoning.* Age 24 years. Duration of known diabetes, 6 months. Weight 6 months ago, 145 lbs. Weight now, 110 lbs. (50 kg.). No quantitative dietary treatment. He was able to work until 2 weeks ago when compelled to stop on account of weakness. No complicating disease. His father was 6 ft. tall and weighed 225 lbs. A father's brother was obese and had diabetes. Inspection shows a tired, emaciated young man. The face has a translucent pallor. *The disease is clearly severe because of the age and the fact that in* 1 *year without artificially imposed under-*

nutrition the diabetes itself has disabled the patient. The same conclusion could be reached by inspection. Examination of the urine shows sugar and a moderate ferric chloride reaction. In view of the latter the patient is questioned closely as to any recent nausea, anorexia or breathlessness and is again examined carefully for increased respiratory rate and a facial flush, but none of these symptoms or signs of acid intoxication is elicited. Treatment is begun as for a *severe diabetes with acidosis but no acid poisoning.*

The patient is weighed and put to bed on a basal maintenance diet. If the basal metabolic rate is normal and he weighs 50 kg. he will require for maintenance about 50 by 25 or 1,250 calories. If he is given .5 to .7 gm. protein per kg. (25 to 35 gm.) and enough fat, this may suffice for protein maintenance. If he receives 2.0 gm. of fat per kg. (100 gm.) the protein and fat together will yield 1,000 to 1,040 calories, leaving him to supply from his tissues the remaining 250 or 210 calories. If he receives 2.5 gm. of fat per kg. (125 gm.), the diet will yield 1,225 to 1,245 calories. In this case we may elect to give .5 to .7 gm. protein and 2.5 gm. fat per kg. If there were any symptoms of acid poisoning it would be safer to give only 2.0 gm. of fat per kg., because with a new case one does not know the actual basal metabolic rate. The writer has seen no accidents with 2.0 gm. per kg., but in two or three instances 2.5 has seemed too high. The diet is prescribed as follows:

Basal Diet for a 50-Kilogram Patient

	Amount	C	P	F
Cream, 20 per cent.....	500 gm.	25	15	100
Eggs, 50 gm. each.....	2	0	12	12
Bacon.....	25 gm.	0	4	13
		25	31	125

To this may be added clear broth to 500 gm., water as desired, tea, coffee, salt, pepper. Give in divided portions during the day, about one-third morning, noon, and night. It will be seen that the diet contains 25 gm. of carbohydrate not theoretically demanded. This could be reduced one-half by using 40 per cent cream diluted with water in place of 20 per cent cream or eliminated by giving the fat in the form of bacon and butter with non-caloric wafers, but the 25 gm. of carbohydrate and the extra 100 calories are of no practical significance and the cream diet is simpler to order, prepare and serve and conducive to greater accuracy since the whole amount can be measured at one time. The diet consists virtually of a pint of cream, two eggs, and an ounce of bacon. Calories 1,345, G = 55.5, FA = 126.8, FA : G = 2.28. It will be noticed that

the ratio for this diet is well over 1.5 and not incompatible with acetonuria, but with a diet of this basal magnitude the quantity of acetone bodies will be virtually the same as though the patient fasted and not more. In subsequent steps as the diet reaches a higher magnitude the ratio will be reduced. It will also be noticed that the diet is very much like the Newburgh-Marsh Diet No. 1, but that the present diet would be calculated for each patient and would have a different value for a 45 or a 55 kg. patient.

On this diet, after 1 to 3 or 4 days, one of two things will occur. Either the urine will became sugar-"free" or the sugar excretion, having fallen day by day, will become virtually constant at some low level, possibly 2 to 10 or more gm. per day. In the latter case one may complete desugarization by cutting the G of the diet as suggested above, or, sparing the patient, one may elect to use insulin. If the excretion is 10 gm., 5 units of insulin may be tried before breakfast, followed the next or the second day by 10 if 5 proves insufficient. Having accomplished the purpose, the insulin may then after a day or two be dropped without a recurrence of the glycosuria. In any case the patient is now on the original basal diet with the urine free of abnormal quantities of sugar. There may be some acetone present, possibly also some aceto-acetic acid. There may be neither. At this stage quantitative estimations of the milligrams of sugar per twenty-four hours by Benedict and Osterberg or Folin and Berglund are highly advantageous and, before beginning additions to the diet, the urinary sugar may be allowed to settle to 10 mg. or less per kg. day (500 mg. for 50-kg. patient), if it will. When it does the blood-sugar percentage will, if taken, nearly always be found normal in a case of this type. In old arteriosclerotic patients the excretion may be found normal while the blood-sugar percentage remains at .17 to .22 per cent and, more rarely, the same may occur in other types of cases. In such situations if the excretion is normal ignoring the blood-sugar percentage rarely leads to regrets, if ever.

We now begin building up the diet a step at a time, raising the value of G by 5, 10 or 15 gm. every third day. One may proceed faster or slower, depending on his estimate of the severity of the case. If the urine became normal promptly on the first diet, more tolerance would be suggested; if slowly and with difficulty, less tolerance. If one were dealing with a moderate instead of a severe case he might choose to raise the G by 25 to 30 gm. at a time to find the tolerance limit without undue loss of time, as will be discussed later. In the present case the indications point to severity.

In raising the diet it is not necessary to keep the ratio of fat and carbohydrate absolutely constant at all stages, nor is it always convenient to do so. The initial diet has a high ratio but a low absolute quantity of fat (2.0 to 2.5 gm. per kg.). In raising the diet one may build

up the carbohydrate first, so that, as the diet increases, the FA : G ratio will subside to the 1.5 level. In the building-up process it is well to have definitely in mind a fixed objective in the form of a final diet with possible alternatives. Then at each step one may add some missing fraction of this diet, with the result that when all are assembled the diet will stand complete. In case the natural tolerance developed by the patient proves too little to permit giving the whole diet without inducing abnormal glycosuria, one may make a virtue of necessity and elect an alternative, or one may use insulin and complete the original program. In the present case, one might visualize some such diet as that outlined below:

DIET OBJECTIVE FOR A 60-KILOGRAM PATIENT

Sections	Table of Values				Foods and Food Groups	Amounts in Grams			
	C	P	F	"G"		Total	A.M.	M.	P.M.
Section I....	12.0	4.0	0.0	14.3	5 per cent Vegetables	400	...	200	200
	10.0	1.0	0.0	10.6	10 per cent Fruits...	100	100	...	...
Totals	22.0	5.0	0.0	24.9					
Section II...	0.0	12.0	12.0	8.2	Eggs (50 gm.).....	2	1	...	1
	0.0	18.8	11.3	12.0	Meat, lean	75	...	75	...
Totals	0.0	30.8	23.3	20.2					
Section III..	0.0	4.8	15.0	4.3	Bacon	30	30	...	...
	20.0	12.0	80.0	35.0	Cream 20 per cent...	400	150	150	100
	0.0	0.0	38.0	3.8	Butter	45	15	15	15
	0.0	0.0	20.0	2.0	Olive Oil	20	...	...	20
Totals	20.0	16.8	153.0	45.1					
Section IV..	24.0	4.1	0.9	26.5	Bread	45	15	15	15
	10.0	2.4	1.1	11.5	Oatmeal, dry wt....	15	15	...	...
Totals	34.0	6.5	2.0	38.0					
Diet Totals	76	59	178	128	FA 187	FA : G 1.47	Calories 2142		

FOOD VALUES BY MEALS

	A.M.					M.					P.M.				
	Amt.	C	P	F	"G"	Amt.	C	P	F	"G"	Amt.	C	P	F	"G"
5 per cent Vegetable.....						200	6.0	2.0		7.2	200	6.0	2.0		7.2
10 per cent Fruit.....	100	10.0	1.0		10.6										
Eggs.....	1		6.0	6.0	4.1						1		6.0	6.0	4.1
Meat.....						75		18.8	11.3	12.0					
Bacon.....	30		4.8	15.0	4.3										
Cream.....	150	7.5	4.5	30.0	13.1	150	7.5	4.5	30.0	13.1	100	5.0	3.0	20.0	8.8
Butter.....	15		0.2	12.8	1.3	15		0.2	12.8	1.3	15		0.2	12.8	1.3
Olive Oil.....											20			20.0	2.0
Bread.....	15	8.0	1.4	0.3	8.8	15	8.0	1.4	0.3	8.8	15	8.0	1.4	0.3	8.8
Oatmeal.....	15	10.0	2.4	1.1	11.5										
Totals.....		35.5	19.3	65.2	53.7		21.5	26.9	54.4	42.4		19.0	12.6	59.1	32.2

All of the foods in this diet are staple and the amounts rational. Thus the 400 gm. of 5 per cent vegetables provide bulk to regulate the bowels, and material for salads at two meals, also protective accessory substances. This quantity of greens belongs in a balanced diet and is enjoyed by the average individual indefinitely. Fruit, besides being antiscorbutic, is eaten habitually by most people at breakfast. The 100 gm. of 10 per cent fruit permits of oranges or a larger quantity of grapefruit for that meal. The average individual will eat one or two eggs per day in one form or another for indefinite periods without tiring. Few will adhere indefinitely to diets containing three to four eggs. The two eggs allow one or two at breakfast or omelettes, custards, etc., at other meals. Meat is an important staple in the ration of most normal persons. The meat rôle is filled by 75 gm. of lean meat, or its protein equivalent in fowl, fish or shellfish. Some people habitually eat less, some more, but 75 gm. will suffice. Bacon at breakfast may be taken for long periods. It may be transferred to the evening meal if preferred. The 30-gm. allowance will be found too large for some patients. Cream for tea, coffee, cereal, ice cream, whipped cream desserts, or diluted with water and drunk as milk or used for the thickening of a tomato soup or the like, is the most generally adaptable form of fat, may be used with the sick or well, contains fat soluble B, etc., and is in all respects desirable. Butter is an essential part of bread and butter but can be used as drawn butter sauce or on eggs or even spread on meat when bread is missing. The oil adds fat and complements greens as French dressing or may be combined with egg as mayonnaise. All patients will not take oil and this is the only uncertain item in the list. It should not be ordered until greens are in the menu. Bread needs no comment. Anything short of 15 gm. at a meal is prone to prove irritating to the patient, but this amount, although small, is practical, allows toast for breakfast, etc. Cereal is a staple breakfast food and 15 gm. make a reasonable serving. There is nothing in such a diet that a patient will not be able to procure when at home or traveling or even at a lunch counter. The diet is arranged in sections numbered I to IV. Each section is made up of kindred foods that permit of wide variation. Thus Section I contains most of the cellulose and is high in accessories. It is chiefly a carbohydrate section with almost no protein or fat. It could be made up to contain 5, 10, or 15 per cent fruits, could consist wholly of fruit or wholly of vegetables, and still, as a section, preserve the same G and nearly the same protein and fat, provided peas and beans were not introduced. Section IV is a carbohydrate grain group. It could be made up with any cereal. Potato could be substituted for the cereal, or for both cereal and bread occasionally, provided G for the section remained the same. It would also be permissible to make exchanges between Section I and IV, but it is wise not to lower Section I permanently. In case of gastro-enteric disorders, however, Section I

may have to be dropped temporarily. In such a case its place may be filled by milk in quantity calculated to give the same G, or more cereal could be used instead of milk to take the place of the vegetables dropped. Section II is the chief protein section, while Section III contains most of the fat. Within Section II, by reducing meat a trifle, place could be made for 3 to 5 gm. gelatin for desserts or, by a greater meat or egg reduction, cheese could be inserted. Section III as a rule will not be altered much because it will be found difficult to give fat in other measurable and palatable forms, but, by allowing fat meat, the olive oil which is not used by all persons can be dropped if desired after completing the period of close observation. The only objection to this lies in the difficulty of measuring the fat of fat meat. The reader will observe other ways in which the above stem diet may be used as a basis for substitution. If the patient, for instance, were a vegetarian, the G of the meat could be developed in vegetables. When working with a diet of this sort it will be found to blend with existing habits in a large percentage of persons. Thus the breakfast is virtually a normal breakfast for the average person with the exception that the bread is limited to a set weight, but a patient who has had some experience with scales will be able to take such a meal with a close approach to quantitative exactness without scales when away from home. The noon meal also may differ but little from that to which a patient is habituated. The evening meal is frankly light. The relative concentration of food at breakfast and the noon meal is favorable if a single daily dose of insulin is to be used. With cases not using insulin, meat may be changed to the evening meal and the lightest meal may fall at noon, especially in the case of business men who eat breakfast and dinner at home and a light lunch in the middle of the day, or the same arrangement may be preferred with a morning and evening dose of insulin. Attention to all of those details spells the difference between a practical régime to which a patient will adhere and an impossible régime that he will violate. It may be noted that, by meals, the diet contains at breakfast fruit, cereal, egg, bread, butter, cream; at the noon meal, greens, meat, bread, butter, cream; at the evening meal, greens, oil, egg, bread, butter, cream, and that the glucose equivalent of the meals runs highest at breakfast, lower at the noon meal, and least at night, roughly as 53, 43, 33. In case insulin is used, this places the greatest supply of glucose within the period of action of a morning insulin injection and favors the possibility of using a single dose per day. If breakfast is at 8, the noon meal at 12, and supper at 6, the last meal falls at the end of the insulin effect. This meal, therefore, if feasible, should be made *low enough to be tolerated without administering insulin.* If this cannot be done, a second dose of insulin before the evening meal may be found desirable.

Returning now to the patient. He weighs 50 kg. but at that weight is weak and disabled. To maintain him with 1,500 calories would merely

sustain his life as an invalid. With 35 calories per kg. (1,750 per day) he could probably work and enjoy life with limitations; but if he were employed he might not be able to retain his position or, if in school, business or a profession, he might not succeed. With 35 calories per kg. at a weight of 60 kg. (2,100 calories per day) he should be able to solve his economic problem. The above diet would then suffice. The protein (61 gm.) would represent 1 gm. per kg. which would serve for protein equilibrium. Even less could and more might be used, but 1 gm. per kg. meets essential needs and permits of more carbohydrate than could be used if the protein were higher. If he developed enough tolerance to use a higher diet safely, protein could then be added without displacing something more essential. In this case, then, we begin by adding to the existing diet:

1. 5 per cent vegetables, 200 gm. at the noon meal. Then if the excretion of sugar remains normal after two days proceed with 2.
2. 5 per cent vegetables, 200 gm., evening meal.
3. 10 per cent fruit, 50 gm., breakfast.
4. 10 per cent fruit, 50 gm., breakfast (3 and 4 could be combined).
5. Meat, 75 gm., noon meal (this step could be divided into 2).
6. Correction of the diet by dropping cream 100 gm., thus bringing the total cream to 400. This subtracts C 5, P 3, F 20, G 8.8 gm. and permits the addition of oatmeal dry weight 15 gm., for which G is 11.4, the total addition being 2.6 gm. G with a lowering of the ratio and calories.

If at this or some earlier stage the glycosuria rose slightly (for example to 1,200 mg.), one could wait and see whether it settled on the next day. If not, one would revert immediately to the basal maintenance diet and make the sugar excretion subside to the normal or conduct the case from then on with insulin. If the last addition caused a more ominous glycosuria one would not wait for it to subside but would stop it at once either by increasing the insulin or by reverting to the original diet. In case of definite glycosuria at this particular stage, one now notes the status of the food supply and finds that it stands C 52, P 56, F 119 with G at 96 gm. At this time, therefore, the tolerance or T of the patient is in the neighborhood of 96 which for a 50-kg. patient means what may be gathered from the following. Twice the carbohydrate of the diet is 104 and half the protein is 28. Twice the carbohydrate plus half the protein is 132. The fat at 119 is below this figure. Therefore, if figured, FA : G would be found less than 1 : 5. One might add fat as olive oil or butter to bring the ratio to 1 : 5. Now the patient weighs 50 kg. and would be receiving only 30 calories per kg. Accordingly for this patient the power to utilize only 96 gm. glucose would spell disaster were it not for insulin. Barring the possibility of a further

increase of tolerance under prolonged care, there would be no bright outlook, and more often than not the tolerance would not rise much after the first three weeks of treatment. After desugarizing on the low diet a second attempt could be made to advance the diet, now taking steps 1 to 4 inclusive at once, followed by a wait, then 5, and a wait, then 6 and a wait, then 7. Possibly one might then proceed slowly without insulin to:

7. Oil, 15 gm.
8. Bread, 10 gm., butter, 5 gm.
9. Bread, 10 gm., butter, 5 gm.
10. Bread, 10 gm., butter, 5 gm., and so on until the diet became complete. But if on taking step 7 the glycosuria recurred one would not then stop but would measure it. If it amounted on the average to but 5 gm. per day the diet could be increased until the sugar excretion became 10 to 15 gm. per day on the average with fair constancy. Then half an hour before breakfast one could give half as many units of insulin as the grams of sugar excreted on the average, calculating that 1 unit of insulin will eliminate 1 to 2 gm. of sugar, and allowing for errors. In this case then 5 to 7 units are given before breakfast. This reduces glycosuria perhaps to 3 to 5 gm., possibly to 500 mg. or normal. Then one may without stopping for complete desugarization again add to the diet, again establish a steady excretion of 10 to 15 gm., and then increase the dose of insulin by half the calculated amount. When the final diet decided upon is in effect and the glycosuria has fallen to a few grams, one finally gives enough insulin to eliminate entirely all abnormal sugar. In the present case with a natural power to utilize 96 gms. glucose and a final diet with G at 129, administered insulin would be carrying some 33 gm. of glucose and this may imply a dose of 10 to 20 units once daily.

Insulin Management.—Every normal individual is in a sense under insulin therapy at all times, the insulin being formed in the body and its dosage regulated by an automatic mechanism. The same is true of every diabetic individual whether receiving additional doses of insulin from outside sources or not. The principles involved in the dietary management of diabetic cases are the same with or without insulin injection. However, the employment of the latter introduces details requiring special consideration.

In the case of a normal individual the supply of insulin from endogenous sources rises and falls automatically with fluctuations of the glucose supply to the body and in the case of a diabetic the same holds true so long as the glucose supply varies below the limits of natural tolerance, but, when this limit is so low that in order to maintain the patient in the non-glycosuric status the diet must be so reduced as to cause partial physical disability by undernutrition, extra insulin may be supplied artificially to prevent this. The conservation and upbuilding of natural

tolerance which before the discovery of insulin was the sole hope of life has become less essential than it was before. *It is still important to conserve natural tolerance as long and to the greatest extent possible because to do so conserves automatic insulin regulatory power,* which is a great convenience, but declines of natural tolerance below certain levels need not now spell disability and death as they formerly did, and it is not necessary or desirable to pay the price of partial disability from undernutrition merely to postpone artificial administration of insulin.

Indications for the Use of Insulin.—As soon therefore as it becomes apparent from the age of the patient, the duration of the glycosuria, the history of the case, and the physical and laboratory findings, that the patient lacks or will shortly lack the power to burn enough glucose to permit him to remain in the non-glycosuric status, on a diet high enough to support his normal life activities and a body weight compatible with health, he should receive the benefit of insulin. Children below the age of ten having developed true diabetes mellitus, no matter how carefully managed by diet adjustment alone, have usually died or approached death within from two to three years. If a few have lived more than seven years, they have done so at the cost of growth, development and much that goes into the normal life of a child. Therefore when a diabetic child reaches the point at which, in order to keep the urine free of abnormal amounts of sugar, it is necessary to reduce the diet to such a degree as to interfere with its normal growth, development, education or well-being, the use of insulin should not be postponed. The same principles apply in the case of adolescents and of young adults with whom a period of curtailed activity may dislocate education or self-supporting work. Finally, in the case of older patients, insulin should be used promptly whenever to refrain from doing so entails disability or undue economic costs. In short, every individual is entitled to enough food to support him in his legitimate work at a body weight compatible with health and a sense of well-being.

In view of the above it will often be decided to place the patient as quickly as possible on the diet calculated to be sufficient to meet legitimate requirements for food and to use insulin as necessary. In severe cases there is advantage for several reasons in placing the patient first on a basal maintenance diet as described above and in building up the ration a step at a time without insulin until the limit of natural tolerance is established: (1) Because one obtains in this way accurate information concerning the individual's own sugar-using power, and concerning the effectiveness of the insulin given. When a new glycosuric patient is placed on a ration differing from that to which he has been accustomed and is at the same time given insulin, the subsequent procedure is apt to become confusing. (2) It is important to familiarize the patient with the basal maintenance diet as one to which he will later have recourse in

case of emergencies such, for example, as acidosis or of becoming detached from his supply of insulin. (3) In educating a patient it is imperative that he understand the principles of diet adjustment and it simplifies instruction to begin with the diets uncomplicated by insulin administration. Otherwise patients tend to gain the impression that the use of insulin is the primary consideration and the diet adjustment secondary instead of vice versa.

However, in building up a diet it will often be found expedient to shorten the period of time required to arrive at the ration set up as the final objective by taking two or more steps at a time if conditions are favorable. Some writers advocate placing patients immediately on their final diets with enough insulin to enable them to carry them. This plan is practical in cases that are not too severe to make it safe and in some cases saves time in hospital. But if the diet given were to induce a high glycosuria and especially acidosis, it would be found necessary to give large doses of insulin to control them and then later reduce the dosage to avoid insulin reaction after the desugarization has permitted a rise of natural tolerance. So that in the end more time may be lost before the case is actually established on a settled basis than if the other process were followed. Moreover, the satisfactory education of the patient which is vitally important requires in itself a certain amount of time and it is a poor economy to balance up a case physically and discharge him hurriedly without the knowledge and experience necessary to insure him against recurrence of the same condition for which he originally presented himself.

The Number and Time of Insulin Doses.—When a dose of insulin is injected subcutaneously it requires time for absorption and the larger the dose injected at one point the longer the absorption time. A dose of 40 units of iletin Lilly of the U 20 or U 40 strength subcutaneously exerts an effect on the sugar utilization for roughly eight hours. Increasing the dosage prolongs the action time. Small doses are absorbed more quickly. A single dose of insulin before breakfast in the morning can easily be made to cover requirements for breakfast and lunch if the morning and noon meals are suitably adjusted. A second dose may then precede the evening meal if necessary. A third dose of insulin between midnight and morning will only be indicated in cases so severe that they develop glycosuria and acidosis in fasting periods without insulin. The fewer the doses employed the less the annoyance to the patient. There is no special object in giving a separate dose of insulin before each meal, one or at most two doses per day sufficing in the great majority of all cases.

Mild or Moderate Diabetes with No Acidosis.—The patient is perhaps 45 to 50 years old and has had glycosuria off and on for from 5 to 8 years. He formerly weighed 200 lbs. and still weighs 165 to 180 lbs.

SHOWING THE NUMBER OF GRAMS OF CARBOHYDRATE, PROTEIN, AND FAT CONTAINED ON THE AVERAGE IN 100 GRAMS OF EACH FOOD (OR IN ONE 50 GRAM EGG) AND THE NUMBER OF GRAMS OF GLUCOSE "G" THAT MAY BE PRODUCED IN THE BODY BY 100 GRAMS OF EACH FOOD, OR A 50 GRAM EGG

Food	Carbohydrate	Protein	Fat	Glucose
Vegetables (5 per cent group)	3	1	0	3.6
Vegetables (10 per cent group)	6	1	0	6.6
Vegetables (15 per cent group)				
Artichokes	15	2	0	16.2
Shelled green peas	15	7	0	19.1
Vegetables (20 per cent group)				
Potato	20	2	0	21.2
Shelled and baked beans	20	7	0	24.1
Green corn	20	3	1	21.8
Fruit (5 per cent grapefruit)	5	1	0	5.6
Fruit (10 per cent group)	10	1	0	10.6
Fruit (15 per cent group)	15	1	0	15.6
Fruit (20 per cent group)	20	1	0	20.6
White bread	53	9	2	58.4
Rye bread	53	9	1	58.3
Bran bread	40	9	1	45.3
Oatmeal (dry weight)	67	16	7	77.0
Farina (dry weight)	76	11	1	82.5
Rice (dry weight)	79	8	0	83.6
Shredded wheat	78	11	1	84.5
Cane sugar	100	0	0	100.0
Clear broth	0	1	0	0.6
Gelatin	0	100	0	58.0
Lean meat (uncooked)	0	20	10	12.6
Lean meat (cooked)	0	25	15	16.0
Fish, halibut, lake trout, whitefish, perch (fresh)	0	18	5	10.9
Fish, salmon (fresh or canned)	0	22	13	14.1
Oysters	4	6	1	7.6
American cheese (pale)	0	29	36	20.4
American cheese (red)	0	30	38	21.2
Whole milk cheese	2	26	34	20.5
Cottage cheese	4	21	1	16.3
Buttermilk	5	3	0	6.7
Skimmed milk	5	3	1	6.8
Whole milk	5	3	4	7.1
Cream 20 per cent	5	3	20	8.7
Cream 30 per cent	5	3	30	9.7
Cream 40 per cent	5	3	40	10.7
Bacon (cooked)	0	16	50	14.3
Butter	0	1	85	9.1
Olive oil (and other oils)	0	0	100	10.0
Butternuts	3	28	61	25.3

GRAMS OF CARBOHYDRATES, PROTEIN, FAT AND GLUCOSE (*Continued*)

Food	Carbohydrate	Protein	Fat	Glucose
Brazil nuts	7	17	67	23.6
Hickory nuts	11	15	67	26.4
Black walnuts	12	28	56	33.8
English walnuts	16	17	63	32.2
Pecans	13	11	71	26.5
Filberts	13	15	65	28.2
Beechnuts	13	22	57	31.5
Almonds	17	21	55	34.7
Peanuts	24	26	39	43.0
Chestnuts	42	6	5	46.0
Green olives	2	1	10	3.6
Ripe olives	4	2	20	7.2
1 egg (50 gm. piece)	0	6	6	4.1
1 egg white	0	4	0	2.3
1 egg yolk	0	2	6	1.8

FOOD ARRANGED ACCORDING TO THEIR APPROXIMATE CARBOHYDRATE CONTENT (AFTER JOSLIN)

Fruits and Vegetables (fresh or canned)

1 per cent-3 per cent	3 per cent-5 per cent	10 per cent	15 per cent	20 per cent
Lettuce	Tomatoes	String beans	Green peas	Potatoes
Cucumbers	Brussels sprouts	Pumpkin	Artichokes	Shell beans
Spinach	Water cress	Turnip	Parsnips	Baked beans
Asparagus	Sea kale	Kohl-rabi	Canned Lima beans	Green corn
Rhubarb	Okra	Squash		Boiled rice
Endive	Cauliflower	Beets		Boiled macaroni
Marrow	Egg plant	Carrots		
Sorrel	Cabbage	Onions		
Sauerkraut	Radishes	Green peas canned		
Beet greens	Leeks			
Dandelion greens	String beans canned	Watermelon	Raspberries	Plums
Swiss chard	Broccoli	Strawberries	Currants	Bananas
Celery	Artichokes canned	Lemons	Apricots	Prunes
Mushrooms		Cranberries	Pears	
		Peaches	Apples	
Ripe olives (20 per cent fat)		Pineapple	Huckleberries	
Grapefruit		Blackberries	Blueberries	
		Gooseberries	Cherries	
		Oranges		

* Reckon average carbohydrate in 5 per cent veg. as 3 per cent—of 10 per cent veg. as 6 per cent.

1 gm.	carbohydrate	yields	4	calories	1 kilogram	= 2.2 lb.
1 "	protein	"	4	"	1 pound	= .45 kg.
1 "	fat	"	9	"	1 ounce	= 30 gm.
1 "	alcohol	"	7	"	1 fluid oz.	= 30 cc.

6.25 gm. protein contain 1 gm. nitrogen. A patient "at rest" requires 25 calories per kg. of body weight.

100 gm.	C	introduces	into	the	body	100 gm.	G	and	0 gm.	F	A.
100 "	P	"	"	"	"	58 "	G	"	46 "	F	A.
100 "	F	"	"	"	"	10 "	G	"	90 "	F	A.

The glucose value of a diet ("G") equals all of the carbohydrate plus 58 per cent of the weight of the protein, plus 10 per cent of the fat, that is

$$G = C + .58\,P + .1\,F$$

The ketogenic acid equivalent of a diet ("F.A.") equals 46 per cent of the weight of the protein, plus 90 per cent of the fat, that is,

$$F.A. = .46\,P + .9\,F$$

When a diet is so arranged that $\frac{FA}{G} = 1.5$, the weight of fat will equal twice the weight of the carbohydrate plus 57/100 of the protein, that is, roughly, twice the carbohydrate plus half of the protein.

$$F = 2C + \frac{P}{2}$$

Except for minor annoyances from polyuria, thirst, a balanitis, a disturbance of refraction or the like, attributable to the excessive circulation and passage of sugar, he has had nothing to complain of except the necessity of dieting. From his age and weight and from the fact that in from 5 to 8 years of careless dieting the disease has not disabled him, one knows that he has no permanently severe diabetes. He could not support a body weight of 175 lbs. and be showing no acidosis unless he had the power to utilize a considerable quantity of glucose. Let it be assumed that he weighs 165 lbs. or 75 kg. and to maintain his weight at work uses 35 calories per kg. per day at least. This implies 2,600 calories per day as a minimum for an active man. To develop this number of calories with no acidosis, he must have the power to burn glucose at least to the extent of 2,600 divided by 17 or 153 gm. In such a case it is unnecessary to begin with a basal diet. One may place him on a diet with G = 150 and note results. If the urine becomes sugar-free, one may raise the dietary G to 175 or higher and so on until one finds his tolerance. If on the first diet he continues to pass sugar it may be measured from day to day and when it becomes virtually constant the tolerance T will be evident. Thus, if on a diet with G = 150 the excretion settles to 5 or 10 gm., one may call T 150—5 or 10, that is, 145 or 140. Then a deep cut of the diet to desugarize may be followed by a quick return to a diet with G at 135 or thereabouts and the building-up process begun at that level. This saves time in

QUANTITATIVE DIET ORDER

PRESBYTERIAN HOSPITAL
Chicago, Illinois

Name_____ Date_____

Room or Ward_____ Diet Ordered by_____

FUEL VALUES C	P	F	"G"	FOODS — The figures below each food show the number of grams of C, P, F and G for 100 grams of the food or 1 egg.	ORDER — TOTAL FOR DAY GM.	Distribution by Meals A. M.	M.	P. M.	REMARKS
				5% VEGETABLES C-3 P-1 F-0 G-3.6					
				10% VEGETABLES C-6 P-1 F-0 G-6.6					
				5% FRUIT C-5 P-1 F-0 G-5.6					
				10% FRUIT C-10 P-1 F-0 G-10.6					
				CLEAR BROTH C-0 P-1 F-0 G-0.6					
				GELATIN C-0 P-100 F-0 G-58.0					
				EGGS, by No. C-0 P-6 F-6 G-4.1					
				LEAN MEAT C-0 P-25 F-15 G-16.0					
				MILK C-5 P-3 F-4 G-7.1					
				CREAM 20% C-5 P-3 F-20 G-8.7					
				BUTTER C-0 P-1 F-85 G-9.1					
				BACON C-0 P-16 F-50 G-14.3					
				OLIVE OIL C-0 P-0 F-100 G-10.0					
				WHITE BREAD C-53 P-9 F-2 G-58.4					
				OATMEAL (Dry Weight) C-67 P-16 F-7 G-77.0					
. 4	. 4	. 9							

Accessory articles: Allow tea, coffee, water, salt, pepper, etc., as desired with reasonable reservations, and, if wanted, also saccharin to .3 gm. daily. Give no special diabetic articles nor non-caloric food substitutes unless ordered.

REMARKS/

CALORIES	
G	
FA	
RATIO	

the hospital and the whole process may require only from eight to ten days.

In case it would seem that with G at 150 the tolerance was 140 and if after reducing the G to 100 the patient still passed sugar to the extent of 5 to 10 gm. per day, it would then seem that T was only 90 to 95. This phenomenon should cause the observer to pause. If T were only 90 to 95 the diabetes would be severe. But the diabetes is obviously not severe, for the reasons given. The history and appearance belie the latter figures. In such a case one may place the patient on a series of diets as suggested under Diagnosis and see how the excretion runs with G at 100—200—300 gm. If on a high G the excretion is moderate and if it takes a very low disabling diet to desugarize, the case is not acting like a typical case of true diabetes mellitus. One may then try the effects of insulin and measure the blood sugar to see whether possibly the case is one of so-called renal diabetes.

Discrepancies of this sort are not always "renal glycosuria." The causes of this phenomenon require further elucidation but in any such case one may feel reasonably sure that the disease is not more severe than it looks and one should hesitate to disable the patient merely to keep the urine sugar-free. If such patients are placed on diets with the G as low but not lower than compatible with good nutrition and are then watched, they will frequently in time become sugar-free. Mental and nervous strain play an important rôle in many. In some there is a pancreas diabetes. In others there may be an hypophyseal anomaly. Some are cases with arterial sclerosis of the extremities, demonstrable by physical examination and by radiogram. In any case they are nearly all non-progressive or very slowly progressive and the patients should not be disabled by the physician without giving the disease a chance to prove its seriousness. All cases in which the age, the duration of the glycosuria, the absence of undernutrition and acidosis suggest mildness and in which it is not possible to demonstrate a sharply definable limit of the power to utilize glucose without glycosuria, are prone to show comparatively little response to insulin and should be set aside for special study as possibly cases that do not demand rigid treatment.

Treatment of the Precomatose Case.—Actual deep coma from which a patient cannot be aroused is a late stage in acid poisoning and recovery is rare. The majority of cases that are described as "comatose" can be aroused and made to swallow liquids and, as Walther observed in animals, deep coma is usually followed in a short time by death. The following refers especially to what may be termed precomatose cases.

Prevention.—This takes precedence of everything else. A diabetic patient showing acetone and a marked ferric chlorid reaction in the urine is potentially a case of acid poisoning and the acidosis should be stopped, or, if for any reason it is not stopped, the physician should

measure the alkali reserve at sufficiently frequent intervals to make sure that he will not be caught napping. If a case is showing a strong ferric chlorid reaction he may be placed on a basal maintenance diet, or empirically .5 to .7 gm. protein and 2.0 gm. of fat per kg. Alkali can be given in doses of 15 gm. q.i.d. without harm. If the urine turns alkaline the dose of alkali may be stopped or the dosage reduced, or, if one is following the plasma CO_2 by Van Slyke's method, he may refrain from giving alkali if he prefers, provided he knows that the alkali reserve is not falling. With a falling reserve, in spite of a basal diet, insulin should be used. But if insulin is not available the alkali should be given *in sufficient quantity*. Rest and the proper diet will make other measures unnecessary in most uncomplicated cases. Individuals under the influence of great nervous or mental strain or of certain types of infection may not respond to rest and diet alone.

Recognition of the early symptoms and signs of acid poisoning are of vital importance. The early symptoms are:

Accentuated Weakness.—The patient nearly always complains early of unusual or unprecedented weakness or of beginning weakness if he has not been weak before.

Increased Frequency of Respiration, Often Increased Frequency and Depth of Respiration.—At first this may not be apparent at rest but slight exertion such as walking may bring it out. Breathlessness on slight exertion in a diabetic with acidosis is not to be explained away lightly.

A Flush in the Face.—The patient may show what appears to be a good color, as though he had been exposed to sun or wind, but a severely ill diabetic should not look too ruddy. He may explain away the sign but it is a signal that should not be ignored.

Gastric Hyperacidity, Nausea.—A patient going into coma may feel that his last meal disagreed with him. He may vomit once or twice. He may only refrain from a meal. He may say that the egg or cream that he ate at breakfast soured in his stomach. He has various explanations to offer. But the physician should not allow him to substitute his own interpretations for a clear statement of the physical feelings and symptoms.

Mental Retardation, Confusion, or Dulling.—These symptoms are followed later by drowsiness.

Pain.—Abdominal distress, abdominal pain, generalized or localized neuritislike pains, are not uncommon and often confuse the patient and doctor. They occur early and subside with advancing intoxication.

When a patient is received with glycosuria and a marked ferric chlorid reaction in the urine with some or all symptoms of acid poisoning, the following steps may be taken: Give at once 20 gm. of the bicarbonate of soda by mouth. Place the soda in an ordinary glass, fill the glass half full of water, swirl the contents and have the patient drink it. Add

another half glass of water to the sediment and repeat. Then give half a glass of clear water and have the patient rinse down any soda sticking to the tongue or fauces. Leave the lips, tongue, and fauces free of soda. Place the patient in bed and order an enema. Give a dose of insulin. The dose may be anywhere from 0 to 60 units, depending on the case. The question of how much to give and how to proceed thereafter requires elaboration.

If a patient is first seen after having been on an abnormally high or unrestricted diet, if there is no infectious element in the case, if he looks fairly well nourished, and if from the history it would seem that the case has not been one of extremely severe diabetes but that it is one of diabetes of only moderate severity thrown into acidosis by too much food or food plus excitement and fatigue, then, *if the symptoms are moderate,* the chances are that diet restriction, rest and relaxation of the bowels with plenty of water and a rational amount of alkali will solve the immediate problem, and in such a case it is not necessary to complicate the situation by giving a large dose of insulin or even any at all. One may decide simply to order a basal maintenance diet and watch the urine, blood and symptoms at 1 to 2-hour intervals. If all goes well one may begin the next day on the diet and proceed with the regular collection of 24-hour urines. In this case insulin is not given until one knows how much will be needed. *The initial diet may consist of .5 to .7 gm. protein and 2.0 gm. of fat per kg. day plus such carbohydrate as happens to be in the cream used as previously described.* But if the case presents on admission severe symptoms of acid poisoning, such as marked mental confusion or dulling of the sensorium with heavy and fast breathing and a dry tongue, or if the patient looks like a severe case of diabetes, or if there is any infectious complication capable of making a moderate case severe for some time, or if the patient is found to have slipped into this condition in spite of a low diet, or, finally, *in case there is any doubt in the mind of the observer as to just what the situation is,* then it is better to err on the safe side and give a decisive dose of insulin at once. For a patient weighing 40 kg., 60 units is certainly not too much (that is, 1.5 units per kg.). This dose subcutaneously will account for the burning, in a severe case, of some 60 to 120 gm. of glucose in 8 to 10 hours or 6 to 15 gm. per hour. Having given the dose in an emergency case one does not know in advance whether the 60 units will prove excessive or not. One must make sure of a marked existing glycosuria before giving it and then collect the urine every hour or two hours to make sure that the glycosuria *does not* disappear. If it shows signs of disappearing, enough sugar must be administered to maintain a glycosuria. Ten gm. of sugar by mouth every hour for 8 to 10 hours following the insulin administration (80 to 100 gm. in 8 to 10 hours against 60 units of insulin) will approxi-

mately suffice to insure the non-occurrence of hypoglycemia and an insulin reaction without depending on such extra sugar as might arise from the tissues (or the basal maintenance diet), and be excreted if no insulin were given. The administered sugar can be given as 50 gm. orange juice plus 5 gm. of sugar or as 150 gm. milk every hour. Some investigators have used larger doses of insulin than 1.5 units per kg. and prefer repeated doses by the intravenous route. The essential principle in the critical case is to give enough insuline early and then to administer enough sugar to keep up steadily a moderate glycosuria. Objection to the large initial dose arises from the fear that having given it one may be unable to administer the necessary sugar by mouth. Against this possibility it is well to have on hand a sterile 50 per cent solution of pure glucose and a 20 c.c. glass syringe with a small long needle for intravenous work, but if a case is carefully nursed intravenous injection will not often be required.

In handling precomatose cases the acidosis is not the only condition requiring attention: (1) *dehydration* and (2) *extreme inanition* may be associated.

1. In extremely undernourished cases feedings should not always be delayed. They may begin early to receive fractions of a basal maintenance diet by mouth. This may proceed hand in hand with the hourly feedings of sugar and need not complicate the program. The diet may be regarded as separate and distinct from the sugar given to counterbalance the insulin on the supposition that the basal maintenance diet will simply cover fasting requirements and leave the catabolism of carbohydrate protein and fat as though no food were given.

2. Great care is required to supply sufficient water without at the same time overtaxing the stomach or bowel. One may usually in a case of average weight give 300 c.c. (1½ glasses) of fluid by mouth hourly for the first 4 to 8 hours or more if thirst demands, but it should be given slowly and with constant watchfulness. It is wise to give 200 to 300 c.c. of salt solution by bowel at some time after the initial enema and repeat 6 hours later unless by that time the case is clearing. With any signs of motor insufficiency of the stomach, it may be well to let the stomach rest for 1 to 2 hours and depend during these hours on hypodermoclysis for the entrance of fluid.

After the initial dose of 20 gm. of soda a second 20 gm. may be given at the beginning of the next hour and perhaps a third an hour later if the air hunger is not declining. Possibly with enough insulin alkali may ultimately prove superfluous. However, 40 to 60 gm. properly given can do no significant harm and if the initial dose of insulin is not decisive alkali may save the day.

To summarize the events let us consider a possible case admitted at

2.30 P. M. He is put to bed and the urine obtained. At 3.00 he may receive insulin and the first 20-gm. dose of soda with water to 300 c.c. Between 3.00 and 4.00 a cleansing enema. At 4.00, 50 c.c. orange juice plus 5 gm. sugar by mouth and if feedings are necessary a fraction of the basal diet amounting to 40 or 50 c.c. At 4.30 the second dose of soda, with 200 to 300 c.c. water; at 5.00 a collection of urine and at 5.00 and 5.30 the same as at 4.00 and 4.30. At 6.00 the feeding of orange juice, etc. At 6.30 soda and water. Total fluids now possibly 800 to 1,000 c.c. (3½ hours). Thereafter, hourly by mouth, orange juice, sugar, no more soda, water by mouth if desired, slowly. At this stage if it seems indicated, one may rest the stomach and give salt solution 250 c.c. by bowel. With no urgent need for food this will have been omitted, leaving only the sugar and water to attend to. After 6 to 7 hours the danger of too much insulin will be passing if the urine still shows sugar. The sugar feedings may then be abated or stopped.

After 6 to 10 hours the situation may be that the patient is free of air hunger and clear in mind, while the urine has become nearly or quite free of aceto-acetic acid and sugar. At this stage the effect of the first dose of insulin will be gone and the danger presents of a return of acidosis and symptoms during the next 8 to 10 hours. One must then watch the patient and the urine sharply at short intervals. A return of the ferric chlorid reaction and glycosuria will call at once for more insulin. One may try now a smaller dose of perhaps 30 to 40 units and continue observations, using sugar if the glycosuria disappears or fades too fast, and more insulin if necessary to stop a rising acidosis. It is desirable as early in the handling of the case as possible to make doses of insulin fall at 7.00 A. M., and at 5.00 to 6.00 P. M., so that a normal day's schedule can be inaugurated for the sake of all concerned. The above schedule may not be followed exactly in any specific case but a plan has its value. A common mistake in handling a patient in acidosis is to permit the diabetic anomaly and the acidosis to overshadow other important indications. In delicate emaciated individuals the wear and tear of the whole experience, the effects of acid on muscles, the labored breathing, the mental excitement, all combine to tax the heart. Cardiac failure is the final cause of death in many cases and it may ensue after the acid has been controlled. The muscles of the diaphragm or those of deglutition or of the stomach or bowel may give out. Accordingly the patient should be spared any unnecessary ordeal and all should be carried out as simply as possible. The room should be kept quiet, uncluttered and uncrowded. The patient should be reassured and encouraged to sleep for from 5 to 30 minutes when possible. Unnecessary intravenous injections, rectal drips, punctures of the arm for blood samples, etc., should be eliminated, and when indispensable they should be done as simply and quietly as possible with the least turmoil and

show of paraphernalia. A definite program permits one to do all that can be done to advantage and to refrain from more.

TESTS AND METHODS

Reduction Tests for Sugar.—The Benedict qualitative test is well known and requires no new description. The writer uses the Haines' test in routine work simply because it is cheap, quick and as serviceable as any. Place 5 c.c. of Haines' solution in a test tube, boil over a free flame, add 2 c.c. of the urine from a marked pipet all at once and boil again briefly. In the presence of much sugar the reaction is complete immediately and if desired one may repeat, using smaller quantities of urine to find the least amount that will yield a positive test, thus gaining an idea of the concentration of the sugar. If 2 c.c. of urine fail to cause an immediate clouding of the reagent, do not prolong boiling but place the test tube under the cold water tap until it is no longer warm to the touch. Then inspect by reflected light. A smoky, greenish, yellowish or a jade green, yellow, or red opacity "like paint" indicates reduction. Disappearance of the blue color is part of the reaction and may occur occasionally without the appearance of a precipitate or colored colloid suspension. Failing to observe a reaction, set the tube aside and inspect it from 5 to 10 or 20 minutes later when a definite reaction may appear. With the test so performed even a normal urine will at times yield a slight reaction. In 24-hour urine, normal excretions for 50-kg. individuals run usually between 300 and 500 to 1,000 mg. of sugar. A faint test will sometimes be caught with 1 gm. to the liter or less; sometimes 1.5 gm. or more will be missed, depending on the amounts of interfering substances in the urine. When using the quantitative test of Benedict and Osterberg or Folin and Berglund it will be noticed that at times positive qualitative tests cause alarm when the total excretion is normal and again fail to detect a rising excretion, but in the urine the test as performed above gives a fair index. The same results are obtainable with Benedict's solution.

Quantitative Tests for Gross Quantities of Reducing Substance.—The polariscope is quick and convenient but inaccurate in the presence of levorotatory β-hydroxybutyric acid and requires a special instrument. The Benedict quantitative test yields dependable results in the hands of skilled operators, but as performed in general gives variable results. Methods that end with an iodometric titration as in the Sachse procedure have advantages. Of these the method of P. A. Shaffer and A. F. Hartman may be recommended for details.

Ferric Chlorid (Gerhardt) Relation.—Take a good-sized test tube two-thirds full of urine and add 10 per cent ferric chlorid a drop at a time. In a normal specimen the drops usually form a light precipitate of the phosphate of iron and in urine containing bicarbonate a dark precipitate of ferric hydroxid with bubbles of CO_2. In urine containing aceto-acetic acid, the drops of ferric chlorid darken on entering the urine but the dark color is quickly replaced by the light color of precipitated phosphate. One continues to add ferric chlorid until all the phosphate is precipitated and a slight permanent darkening begins. *Then pour the contents of the tube on a folded filter* and catch the filtrate. If turbid at first, empty the turbid filtrate back on to the filter and catch the clear filtrate. This should be light or but slightly darkened. Filtration removes the obscuring phosphate precipitate. Then to the clear filtrate add 10 per cent ferric chlorid a drop at a time until one more drop causes no further deepening of the color. In the presence of aceto-acetic acid the first drop of added ferric chlorid causes perceptible darkening without loss of clarity. Successive drops cause progressive deepening of color if there is much aceto-acetic acid. In this way only may one develop and see the faintest reaction and the maximum color and be in a position to compare colors in successive samples. Some urine contains so little phosphate that filtration is unnecessary. The color developed shades from a faint reddish brown to a deep garnet and may be so deep as to resemble purple grape juice. A slight brownish darkening is not due necessarily to aceto-acetic acid. If very dark or purplish rather than garnet or "Bordeaux" wine colors develop, dilute one-half and heat over a free flame. The color due to aceto-acetic acid then fades slowly. The color produced by aspirin or other drugs containing salicylic or phenol groups tends to persist.

Nitroprussid Test for Acetone..—Select a narrow centrifuge tube. Reduce in a mortar a gram or two of sodium nitroprussid to a fine powder. Keep this in a small corked phial with a small spatula such as a toothpick thrust in the cork. Have a bottle of ammonium sulphate crystals and ammonia water. To perform the test, add 6 drops of urine to the centrifuge tube, then finely divided ammonium sulphate crystals enough to supersaturate the urine, and a little of the nitroprussid powder on the end of the spatula or a knife point. It dissolves at once. Then add 6 drops of ammonia water. Layers form, but the whole may be shaken. In the presence of a considerable amount of acetone a deep purple develops. Smaller traces cause lighter shades. The test so performed is extremely delicate and, if always done in the same way, gives a very good conception of the concentration of acetone. Keeping the nitroprussid in powdered form is economical and insures always a freshly prepared solution.

Formalin Titration for Ammonium.—Select two 100 c.c. Erlenmeyer flasks I and II. To I add urine 10 c.c. from a pipet, 50 c.c. of distilled water from a graduated cylinder and 5 drops of 1 per cent alcoholic phenolphthalein. To II add 4 or 5 c.c. of formalin, 50 c.c. of distilled water and 5 drops of the phenolphthalein. Place I and II under a buret containing .1 NNaOH or KOH and bring each to the first permanent pink blush without reading the amounts of alkali used. Then pour the contents of II into I. The mixture of these two faintly alkaline solutions becomes acid instantly, losing the pink tint. Now set the buret and titrate the mixture, adding alkali until the first permanent pink tint returns. Read the buret and note the number of cubic centimeters of .1 N alkali required.

Calculation.—Assuming that 16 c.c. were required, multiply 16 by 0.0018 to give 0.0288 which is the number of grams of NH_4 in the quantity of urine used (in this case 10 c.c.). Multiply 0.0288 (in this case) by the number necessary to give the total grams of NH_4 in the twenty-four hours' urine; thus, if the day's amount were 2,000 c.c. multiply 0.0288 by 20 to give 0.5760, that is, 0.58 gm. NH_4 in twenty-four hours.

CO_2 Combining Power of Plasma.—The Van Slyke method of determining the CO_2 combining power of the plasma is described by Van Slyke and Cullen, Hawk, and Joslin, in publication given in the list of references.

Stanley R. Benedict-Emil Osterberg Method for Determination of Sugar in Normal Urine.—Fifteen c.c. of urine are treated with about 1 gm. of bone black and the mixture shaken vigorously occasionally for a period of five to ten minutes. The mixture is then filtered through a small dry filter paper into a dry flask or beaker. The volume of this filtrate to be used in the determination will depend upon its sugar content, but should never exceed 3 c.c. Such a volume should be used as will contain about 1 mg. of sugar. The proper volume of the urine filtrate is measured into a large test tube which is graduated at 25 c.c. and, if the volume used was less than 3 c.c., enough water is taken to make the volume exactly 3 c.c. Now add exactly 1 c.c. of 0.6 per cent picric acid solution (best prepared from dry picric acid) and 0.5 c.c. of 5 per cent sodium hydroxid solution. Just before the tube is ready to be placed in boiling water add 5 drops of 50 per cent acetone (this should be prepared fresh every day or two by diluting some pure acetone with an equal volume of water) taking care that the drops fall into the solution and not on the sides of the tube. Shake the tube gently to mix the contents and place immediately in boiling water and leave for from twelve to fifteen minutes. The standard solution should be simultaneously prepared by treating 3 c.c. of pure glucose solution (containing 1 mg. of the sugar) exactly as described for the unknown

solution and heated simultaneously. The solutions are then compared with the standard in a colorimeter. Normal 24-hour urines contain on the average 10 mg. sugar per kg. of body weight but may vary from 5 to 15.

Folin-Berglund Method for Estimation of the Sugar in Normal Urine.—To 5 c.c. of urine add 5 c.c. tenth normal sulphuric acid and 10 c.c. of water. Add 1.5 gm. of Lloyd's reagent and shake gently for two minutes. Filter. Two c.c. of the filtrate is the usual amount used for concentrated urines. With less concentrated specimens, take 10 to 15 c.c. and reduce the amount of water used.

The method is then carried on as in the method of Folin and Wu for sugar in blood after the preparation of the blood filtrate as described below.

Preparation of Protein-free Blood Filtrates.—The blood should be collected over finely powdered potassium oxalate, about 20 mg. for 10 c.c. of blood. It is important not to use unnecessarily large amounts of oxalate because the excess makes the complete coagulation of the proteins more difficult and also interferes more or less with the uric acid precipitation.

Reagents required for the precipitation of the proteins:

1. A 10 per cent solution of sodium tungstate. Some sodium tungstates, though labeled c.p., are not serviceable for this work. They usually contain too much sodium carbonate. The c.p. sodium tungstate made by the Primos Chemical Company is satisfactory.

2. A two-thirds normal sulphuric acid solution, 35 gm. of concentrated c.p. sulphuric acid diluted to a volume of 1 liter, will usually be found to be correct; but it is advisable, indeed necessary, to check it up by titration. The two-thirds normal acid is intended to be equivalent to the sodium content of the tungstate, so that when equal volumes are mixed substantially the whole of the tungstic acid is set free without the presence of an excess of sulphuric acid. The tungstic acid set free is nearly quantitatively taken up by the proteins and the blood filtrates obtained are therefore only slightly acid to Congo-red paper.

Transfer a measured quantity (5 to 15 c.c.) of oxalated blood to a flask having a capacity of fifteen to twenty times that of the volume taken. Lake the blood with 7 volumes of water. Add 1 volume of 10 per cent solution of sodium tungstate ($Na_2WO_4, 2H_2O$) and mix. Add from a graduated pipet or buret, slowly and with shaking, 1 volume of two-thirds normal sulphuric acid. Close the mouth of the flask with a rubber stopper and shake. If the conditions are right, hardly a single air bubble will form as a result of the shaking. Let stand for five minutes; the color of the coagulum gradually changes from bright red to dark brown. If this change in color does not occur, the coagula-

tion is incomplete, usually because too much oxalate is present. In such an emergency the sample may be saved by adding 10 per cent sulphuric acid, one drop at a time, shaking vigorously after each drop, and continuing until there is practically no foaming and until the dark brown color has set in.

Pour the mixture on a filter large enough to hold it all. This filtration should be begun by adding only a few cubic centimeters of the mixture down the double portion of the filter paper and withholding the remainder until the whole filter has been wet. Then the whole of the mixture is poured on the funnel and covered with a watch glass. If the filtration is made as described, the very first portion of the filtrate should be clear as water and no refiltering is necessary.

Simplified and Improved Method for Determination of Sugar in Blood.—The reagents for this method are prepared as follows:

1. *Molybdic Acid and Sodium Tungstate.*—Transfer to a liter beaker 35 gm. of molybdic acid and 5 gm. of sodium tungstate. Add 200 c.c. of 10 per cent sodium hydroxid and 200 c.c. of water. Boil vigorously for twenty to forty minutes so as to remove nearly the whole of the ammonia present in the molybdic acid. Cool, dilute to about 350 c.c., and add 125 c.c. of concentrated (85 per cent) phosphoric acid. Dilute to 500 c.c.

2. *Alkaline Copper Solution.*—Dissolve 40 gm. of pure anhydrous sodium carbonate in about 400 c.c. of water and transfer to a liter flask. Add 7.5 gm. of tartaric acid, and when the latter has dissolved add 4.5 gm. of crystallized copper sulphate. Mix and make up to a volume of 1 liter. If the chemicals used are not pure a sediment of cuprous oxid may form in the course of one or two weeks. If this should happen, remove the clear supernatant reagent with a siphon, or filter through a good quality filter paper. Our reagent seems to keep indefinitely. To test for the absence of cuprous copper in the solution, transfer 2 c.c. to a test tube and add 2 c.c. of the molybdate phosphate solution; the deep blue color of the copper should almost completely vanish. In order to forestall improper use of this reagent, attention should be called to the fact that it contains extremely little alkali, 2 c.c. by titration (using the fading of the blue copper tartrate color as an indicator), requiring only about 1.4 c.c. of normal acid.

3. *Standard Sugar Solutions.*—Three standard sugar solutions should be on hand: (1) a stock solution, 1 per cent dextrose or invert sugar, preserved with xylene or toluene; (2) a solution containing 1 mg. of sugar per 10 c.c. (5 c.c. of the stock solution diluted to 500 c.c.); (3) a solution containing 2 mg. of sugar per 10 c.c. (5 c.c. of the stock solution diluted to 250 c.c.). The invert sugar solution has the advantage that it can be easily prepared from cane sugar, which is pure.

The keeping quality of such solutions should be less good than those made from glucose, but we have encountered no trouble on that score. When good quality glucose is available, it is, of course, the one to use. The diluted solutions should be preserved with a little added toluene or xylene; it is probably better not to depend on such diluted solutions to keep for more than a month, but the stock solution should keep indefinitely.

For accurate work the determination is best carried out in special test tubes having a bulb at the bottom, the capacity of which is slightly less than 4 c.c. A constricted region about 8 mm. in diameter by 4 cm. in length connects this bulb with the upper portion of the test tube. The tube is also usually graduated to 25 c.c. Such tubes are supplied by E. Greiner Company, New York, and by A. H. Thomas Company, Philadelphia.

Procedure.—Prepare the protein-free blood filtrate from 2 c.c. or more of the blood as described in the preceding section. Transfer 2 c.c. of the tungstic acid blood filtrate to a blood-sugar test tube, and to two other similar test tubes (graduated at 25 c.c.) add 2 c.c. of standard sugar solution containing respectively 0.2 and 0.4 mg. of dextrose. To each tube add 2 c.c. of the alkaline copper solution. The surface of the mixtures must now have reached the constricted part of the tube. If the bulb of the tube is too large for the volume (4 c.c.) a little, but not more than 0.5 c.c., of a diluted (1:1) alkaline copper solution may be added. If this does not suffice to bring the contents to the narrow part, the tube should be discarded. Test tubes having so small a capacity that 4 c.c. fills them above the neck should also be discarded. Transfer the tubes to a boiling water bath and heat for six minutes. Then transfer them to a cold water bath and let cool, without shaking, for two to three minutes. Add to each test tube 2 c.c. of the molybdate phosphate solution. The cuprous oxid dissolves rather slowly if the amount is large, but the whole, up to the amount given by 0.8 mg. of dextrose, dissolves usually within two minutes. When the cuprous oxid is dissolved, dilute the resulting blue solutions to the 25 c.c. mark, insert a rubber stopper, and mix. It is essential that adequate attention be given to this mixing because the greater part of the blue color is formed in the bulb of the tube. Read in colorimeter and calculate sugar in terms of the standard used.

Insulin Technic.—It is well to use 27 to 29 gage hypodermic needles ¾ to 1 inch in length with 1½ to 2 c.c. glass syringes. The needles are inserted full length *under* the skin and cutaneous fat into a loose space. Pressure during injection is fastidiously avoided. The solution is warmed before injection. A flexor or adductor surface where the skin is thin and elastic and the subcutaneous space commodious is sometimes con-

venient. Care is taken to avoid raising a lump or welt at any time during injection. The needle point should be freely movable under the skin and the skin freely movable over the point of the needle. If it lies *in* the skin or in the firmer tissues beneath, pressures may arise during injection with unnecessary pain, soreness, scarring, etc. Patients are taught to give their own injections whenever feasible. The thigh is then usually selected. If resistance is met the needle is readjusted until the fluid flows in with no more than the gentlest pressure of a finger tip on the plunger. Plenty of time should be taken.

REFERENCES

Allen. Treatment of Diabetes Mellitus, Nelson's Loose Leaf System.

Benedict, Stanley R., and Osterberg, Emil. Journ. Biol. Chem., xlviii, 51-59, Sept., 1915.

Folin, Otto. Laboratory Manual of Biological Chemistry, 1920 ed., 179, 180.

Folin, Otto and Berglund. Journ. Biol. Chem., li, 209-213, March, 1922.

Folin, Otto, and Wu, Hsein. Ibid., xli, 367-375, March, 1920.

Hawk. Physiological Chemistry, 5th ed., 325.

Shaffer, P. A., and Hartman, A. F. Journ. Biol. Chem., xlv, 365-405, Jan., 1921.

Van Slyke. Ibid., xxx, 347, 1917.

Van Slyke and Cullen. Ibid., xxx, 289, 1917.

CHAPTER XXIII

OBESITY

EDWIN A. LOCKE

REVISED BY ERWIN G. GROSS

Introduction.—Obesity is a condition characterized by the accumulation of more than the physiological amount of body fat. The term is an indefinite one, and it is not always easy to determine precisely the point at which the degree of corpulence becomes abnormal. It should be regarded rather as a symptom of disordered metabolism than as a clinical or pathological entity, unless causing definite functional trouble of the organs or the nervous system. Obesity requires treatment only when such symptoms are present.

Under conditions of health, adipose tissue is found in practically all animal tissues subcutaneously as well as within the cavities of the body. Fat is also stored in the muscles and liver. The distribution, however, is not necessarily proportionate, and varies greatly in different individuals. Fat tissue exists normally in the ratio of approximately 50 gm. per kg. of body weight, that is, about 4 kg. for a person weighing 80 kg.

Bishoff gives the composition of the human body as follows:

	Per Cent
Water	59
Protein	9
Collagenous material	6
Fat	21
Salts	5

Fat, therefore, comprises roughly one-twentieth of the body weight in adult males. The ratio is somewhat greater in females. Its percentage may, however, vary widely from the above, without the condition being considered actual obesity. In some cases an accumulation of even 4 to 6 kg., unless accompanied by functional disturbances, may be regarded as within normal limits.

The following tables give a general idea of the average weights of males and females of different heights and according to age periods:

TABLE OF HEIGHT AND WEIGHT AT VARYING AGES*

MALES

Ages	15-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69
Height	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight
5-0	120	125	128	131	133	134	134	134	131	...
5-1	122	126	129	131	134	136	136	136	134	...
5-2	124	128	131	133	136	138	138	138	137	...
5-3	127	131	134	136	139	141	141	141	140	140
5-4	131	135	138	140	143	144	145	145	144	143
5-5	134	138	141	143	146	147	149	149	148	147
5-6	138	142	145	147	150	151	153	153	153	151
5-7	142	147	150	152	155	156	158	158	158	156
5-8	146	151	154	157	160	161	163	163	163	162
5-9	150	155	159	162	165	166	167	168	168	168
5-10	154	159	164	167	170	171	172	173	174	174
5-11	159	164	169	173	175	177	177	178	180	180
6-0	165	170	175	179	180	183	182	183	185	185
6-1	170	177	181	185	186	189	188	189	189	189
6-2	176	184	188	192	194	196	194	194	192	192
6-3	181	190	195	200	203	204	201	198	196	195

FEMALES

4-11	112	115	117	119	122	125	128	128	126	...
5-0	114	117	119	122	125	128	130	131	129	...
5-1	116	118	121	124	128	131	133	134	132	...
5-2	118	120	123	127	132	134	137	137	136	...
5-3	121	124	127	131	135	138	141	141	140	...
5-4	124	127	130	134	138	142	145	145	144	...
5-5	127	131	135	139	143	147	149	149	148	...
5-6	130	135	139	142	146	151	153	153	152	...
5-7	134	139	143	147	150	154	157	156	155	...
5-8	138	143	147	151	155	158	161	161	160	...
5-9	142	147	151	155	159	163	166	166	165	...
5-10	146	151	155	159	163	167	170	170	169	...

* These tables are published through the courtesy of Dr. Frederick L. Hoffman, statistician of the Prudential Insurance Company of America. The figures for males are based on 74,162 and for females on 58,855 applicants for life insurance.

Physiology.—In order effectively and intelligently to treat the obese, it is absolutely essential to start with a clear understanding of the physiology of the condition, since the treatment is largely based on the principles of nutrition.

The food requirements for the healthy individual leading an ordinary active life are, roughly, 40 calories per diem per kg. of body weight, or

for one weighing 80 kg. (176 pounds) a total of 3,200 calories. There is no exact proportion of the three nutritive constituents furnishing this fuel value which may be taken as a standard, but studies of various American diets show that the average is approximately as follows:

	Calories
100 gm. protein	410
150 gm. fat	1,395
350 gm. carbohydrates	1,435
	3,240

It is evident that these food requirements vary within wide limits depending on many factors. For example, the necessary calories are markedly influenced by the amount of energy expended, the above requirements of 3,200 calories being reduced nearly one-half when the individual is completely at rest. Many other factors, such as the weight, area of skin surface, type of life with respect to the expenditure of heat and energy, age, sex, climate, seasons, etc., exert a very marked influence on the fuel needs. Furthermore, the natural daily variations in the diet and appetite must also result in a considerable variation in its total caloric value. Even such slight departures from the normal as cannot be appreciated by the individual may readily cause an increase or diminution in the food value of several hundred calories. For example, 100 calories is represented by one small lamb chop, one average size boiled potato, three large prunes, one large orange, one ordinary pat of butter, one slice of bread, or one small glass of milk.

It is extremely doubtful if, under ordinary condition of life in health and following the dictates of appetite, we ever eat too little food during a given day. Nature's method seems to be a certain degree to use the human body as a storehouse for fuel. When the diet contains more food than is necessary to answer the demands for heat, energy, and internal work, a certain portion of the excess is preserved in the body in the form of fat. During a period of insufficient nutrition this store of fat can be drawn on and utilized by oxidation to furnish energy either in the form of heat or muscular work. In the great majority of individuals this accumulation of adipose tissue does not exceed the normal limits of approximately one-twentieth of the body weight, but in others the excess of food leads to the deposit of an excessive amount.

Foods through oxidation in the body serve two functions, namely, as tissue builders and as sources of energy (muscular work, internal work, and heat). The various food constituents meet these needs in varying degrees. The formation and repair of body tissues are derived solely from the protein, water, and mineral matter. Fats and carbohydrates

under no consideration serve this function. It is seen, therefore, that the proteins represent the most important form of food and are absolutely essential in considerable quantity to maintain life.

That body heat and energy under normal conditions are largely derived from the carbohydrates and fats is generally accepted, but when present in excess of the quantity needed for tissue repair, the protein is also metabolized to the same end. Indeed, many physiologists believe that the body cells may derive their energy from all with equal facility provided the supply is adequate. Rubner has shown that the various food constituents can be compared with reference to their value as sources of heat in accordance with their caloric value. The comparison is made on the basis of the quantity of each necessary when oxidized in the body to raise 1 kg. of water from 0° to 100°. The resulting weights he calls their "isodynamic value." He gives the following summary:

	Calories Yielded by 100 Grams	*Isodynamic Values*
Fat	942.3	100
Cane sugar	400.1	235
Bread	280.2	336
Meat	96.3	978
Milk	67.3	1,400

In general, since 1 gm. of protein or carbohydrate oxidized in the body yields 4.1 calories and 1 gm. of fat 9.3 calories, it follows that 1 gm. of fat is equivalent to approximately 2.3 gm. of either carbohydrate or protein. Usually the energy required is provided entirely or in large part by combusion of the fats and carbohydrates, thus leaving the protein to answer the demands for tissue building. It is evident, then, that, while neither the fats nor carbohydrates can replace protein as regards this function, both may, by reason of the greater readiness with which they are oxidized to yield energy, spare the proteids for this purpose.

The adipose tissue of the body is chiefly formed directly from the fats and indirectly from the carbohydrates ingested, but in larger proportion from the latter. The carbohydrates are absorbed into the blood as dextrose, which is then converted into glycogen, and as such stored in the liver and muscles. In similar manner, protein if in excess may also be a source of fat, as in the case of the carbohydrates, probably going through the intermediate steps of glycogen formation. Under ordinary conditions of health there is good evidence to the effect that but little, if any, fat is formed from this foodstuff.

A word should be said regarding alcohol. When taken in small amounts, that is, a few ounces daily, it is oxidized in the body exactly as

in the case of the carbohydrates and fats, to furnish energy, and hence similarly may spare the proteids. Unlike the other food constituents, alcohol cannot form body fat. It is important to remember that, while alcohol in small quantities is a food, in larger amounts it acts as a drug, which action may outweigh its effects as a nutrient, since it may interfere with the digestion and assimilation of other foods.

To summarize, then, the functions of the various foods are as follows: to supply energy in the form of muscular work or heat; to build or repair body tissue; and to regulate the body processes. Energy may be derived from fats, carbohydrates, and proteins. Fat tissue is formed directly from fat ingested, carbohydrates and proteins under certain circumstances.

Certain facts regarding metabolism during a period of prolonged fasting are of the greatest importance, because of the direct application to principles laid down later for the regulation of the diet during a reduction cure. Since during starvation no carbohydrates are ingested, and the reserve of glycogen is so small as to be of no consequence, it follows that the sources of energy during fasting must be from the body protein and fat. Lusk states that, in the case of a normally nourished individual, the fasting metabolism is practically constant, 13 per cent of the total energy being furnished by the protein and the remaining 87 per cent from the fats. From the results of a large number of experimental studies Lusk makes the deduction that "the quantity of protein metabolism in starvation depends upon the amount of fat in the body." When the body fat is abundant a much smaller proportion of protein is used than otherwise. In the absence of fat the energy may be entirely derived from the burning of protein. In any case, the destruction of protein constantly increases as the amount of available fat diminishes. As emphasized by the same writer, it also follows that the loss in body weight is much greater when the energy is derived chiefly from the protein rather than from the fat.

In the reduction of weight it is obviously important to bring about a loss of the panniculus adiposus without a loss of body protein; in other words, to preserve nitrogen equilibrium while the carbon equilibrium is destroyed. Experiments have shown that this is readily accomplished (Lusk).

Some consideration of heat loss is necessary as bearing especially on the methods employed in stimulating the metabolism in the treatment of the obese. In general, metabolism is increased by external cold and decreased by external heat, in accordance with the need for the maintenance of a constant body temperature. The temperature of the cells of the organism is then maintained through the regulation of metabolism, which Rubner has shown to be proportional to the area of the surface of the body. The body loses heat by (1) conduction and radiation; (2) evaporation of water from the lungs and skin; (3) warming of the in-

gested food; and (4) warming of the inspired air (Lusk). By far the most important paths through which heat is lost are the evaporation of water and conduction and radiation. It is clear that the degree of loss must depend on many internal as well as external factors, too numerous to discuss in this chapter.

At normal or low temperature, and in moderately dry air, the excretion of water through the skin by the obese does not differ from the normal (Rubner). Of special interest is the fact that, in hot climates with high humidity, the obese can dissipate the heat of metabolism by evaporation of perspiration less easily than thin people, and therefore work less advantageously. The amount of water thrown off by the skin is much greater than that of normal individuals, and von Noorden states that as much as from 3 to 4 liters may be excreted in a few hours. Thus it will be seen that fat people are limited in the degree to which they can regulate the heat of metabolism through radiation, with the result that under certain conditions there may be increased internal heat and great discomfort.

Von Noorden says:

"The ingestion of a quantity of food greater than that required by the body leads to an accumulation of fat, and to obesity, should the disproportion be continued over a considerable period."

He groups the causes of obesity under three heads, as follows: (1) an increased food supply with normal energy expenditures; (2) a normal food supply with diminished energy expenditures; and (3) a combination of the two. While seemingly a very satisfactory grouping, in many cases of obesity it is not possible to determine from which combination the condition arises. That there is in all cases of this condition an excess of food over the quantity needed to answer the body's needs is evident for the reason that, as shown above, food is deposited as adipose tissue only under such conditions. In other words, the disproportion between the intake of food and that metabolized is always present. Such an excess need not be great, or even regular, for, if only slight but long continued, an abnormal amount of fat tissue may be formed. Simple calculation will show that an average excess of 100 calories per day will mean an accumulation of many pounds of fat in the course of a few years. Fat tissue is normally present in the body, and why, with the abundant diet of the well-to-do, a condition of obesity does not always develop is difficult to explain. Clearly other factors than the above mentioned must necessarily be present.

Since the loss of body heat is directly proportional to the body surface, and this area is relatively less in fat people, it should follow that a relatively smaller amount of food per kilo of weight will suffice to

maintain the obese than the normal individual. Hence, an amount of food sufficient to answer the needs of the well may, in the case of the former class, be slightly in excess of the body needs, and sufficient to cause a further accumulation of fat. As is well known also in this class of individuals, there is a general tendency to inactivity with a consequent decrease in the caloric needs. The sedentary indoor life with lessened muscular activity in these cases, so often observed, results in a greater or less depression of general vitality. That this may lead to a lessening of the power of the body cells to oxidize food can hardly be doubted. Although the metabolism in the obese is usually said to be normal, von Bergmann recently proved that, in some cases at least, metabolism is diminished. This abnormal condition von Noorden has termed "the slowing of metabolism," by which he means to indicate that the cells use less fuel than normal in providing energy in the form of external work. In such a condition may be found the interpretation of the so-called "constitutional tendency" present in so large a percentage of cases. Unquestionably in many instances the predisposition to obesity can be analyzed to mean a lack of the proper amount of exercise with an increased quantity of food. This idea is strengthened by the fact that the increase in weight very often comes at the time of life when these factors are especially potent. The predisposition must often be regarded as strictly hereditary. Oertel believes that at least 50 per cent of all cases fall in this class. In a large series of cases tabulated from among private patients I found that nearly 70 per cent give a definite family history of excessive weight sufficient in degree to suggest the probability of an inherited tendency to the condition on the part of the patient.

The increase in nitrogenous metabolism observed in Graves' disease first suggested the use of thyroid extract in the treatment of obesity. Precisely how the gland exerts its influence on the general metabolism is not known, but many observations have shown that in such conditions as myxedema, which are due to lessened activity of the thyroid, the metabolism is lowered, while in such diseases as exophthalmic goiter, in which there is present an increased activity of the gland, the metabolism is strikingly stimulated. Effects exactly similar to the latter have been repeatedly observed to follow the ingestion of thyroid extract in both man and animals. The principal effect is in the increased oxidation of protein.

Much has been written regarding the relation of body weight to the secretions of the sexual organs. It has long been held that castration in either sex tends to induce a condition of increased adipose tissue. This, however, seems very doubtful in the light of recent experiments. The frequently observed increase in weight at puberty, after the menopause, and following lactation likewise does not prove any definite relation to sexual functions. The accompanying hyperalimentation with the tendency

to indulgence in fat-forming foods and diminished bodily activity appear to be more rational causes.

Prophylaxis.—Prophylaxis, though of the utmost importance, is often extremely difficult. While relatively simple to carry out, it is frequently quite impossible to convince people, especially those in good health, of the symptoms which will later follow, and of the consequent necessity for the adoption of measures directed to the limiting of the adipose development. Until the degree of obesity becomes extreme, or until late in its course severe symptoms appear, the corpulent are seldom willing to submit to the necessary régime of treatment. Prevention of obesity is of greater importance than the treatment of the condition. With the appearance of the early signs of increase in fat tissue, the individual should be warned of the probably further increase and the symptoms and complications which will follow. The causes can usually be found in the mode of life with a lack of muscular activity, or in a diet which oversupplies the caloric needs of the system. The principles to be followed are discussed under treatment. In every case the measures advised should be chosen with especial reference to the indications of the individual case.

Prophylaxis is especially indicated in the offspring of the very obese, and should be undertaken even in the early years. In the case of children, however, the greatest care should be exercised in the restriction of the diet, lest the general nutrition become impaired. By a careful limiting of the fat-forming foods and regulation of exercise in the open air, undue accumulation of fat can, as a rule, be successfully prevented. Residence in the country and in summer at the seaside are desirable as favoring an outdoor life.

With the approach of middle life in both sexes the tendency to corpulency is noted most frequently, and it is at this period that prophylaxis is most important. All excesses in eating and drinking should be prohibited, and the individual encouraged to live an active life as much as possible in the open air. Out-of-door sports, such as tennis, golf, riding, rowing, and especially walking are of great advantage. Sea bathing affords one of the most ideal forms of exercise.

TREATMENT

Choice of Cases.—One of the most important considerations is the decision as to the suitabiliy of a given case for a reduction cure. Not all fat people should attempt to lose weight. Nature never meant that all should conform to a common standard in this regard. It is very questionable if those who are only moderately fat and who show no symptoms should be treated, provided they live a rational life as regards diet and

exercise. A moderate degree of corpulence is consistent with perfect health.

The very young, even if they show an extreme degree of overweight, should practically never be placed on a rigid régime. It is almost impossible under such circumstances during the early years of life to provide surely against a retardation of development. One should be content with instituting a routine of diet and exercises to protect against further increase in weight. The aged are also unfavorable cases. A considerable loss in weight almost certainly leaves them much older in appearance, and often actually hastens decay. Another unfavorable class includes those who have been fat since early years. If reduced at all, it should be done very slowly and with extreme care.

The discussion as to the advisability of reducing weight should always be influenced by the condition of the kidneys, heart, circulation, and general vitality. Although organic disease is usually a contra-indication to treatment, it should not be forgotten that it is sometimes such a condition as this which makes a reduction cure imperative. The presence of diabetes or tuberculosis is practically always an absolute contra-indication.

The most favorable cases are those under middle life, who are in good general health, and in whom the condition of obesity is of relatively short standing. Men, as a rule, yield to treatment more readily than women.

General Considerations.—If carried out according to scientific principles and with careful attention to the minutest details, the cure of obesity is exceedingly simple in the great majority of cases. Indeed, the response to rational treatment is often so prompt that the danger most necessary to be guarded against is a too rapid reduction. The physician very commonly must resist the demands of his patient that the loss in weight should be more rapid. Frequently the desire is expressed to complete the course of treatment in a few weeks, notwithstanding the fact that the gain in weight is the result of many years of gradual increase. The purpose of the treatment is to reduce the body weight through the loss of fat tissue, and not the oxidation of body protein with loss of strength, which inevitably results if the rate of decrease is excessive. The reduction should always be accompanied by an increase of strength and general vitality. Any symptom of weakness is always to be interpreted as a danger signal and a certain sign that the régime is faulty in some respect. The unfortunate results of bad treatment are responsible for the idea so prevalent that reduction cures are always attended with grave dangers. In the minds of the laity almost every possible bodily ill can be attributed to bad effects of such treatment. If the treatment be intelligent and temperate, one need never fear the slightest unfavorable results. Furthermore, the decrease in weight leads to important changes in the general metabolism, and especially the work of the internal organs. This read-

justment must obviously be brought about gradually. The rate of loss depends on the total weight of fat to be destroyed. If only 5 to 10 pounds, it makes little difference how rapidly it is removed. In the case where the amount is greater, the rate of loss should not be more than 6 to 8 pounds per month, and then for a period of only two or three months. With the very obese the amount should not exceed 40 to 50 pounds in a single year, and even that amount only in robust individuals who improve in health month by month with the reduction.

My own plan is to continue the treatment for short periods of usually about two months with intervals of a few weeks to two months between, during which the diet and exercises are so regulated as to maintain the weight so far as possible at a constant level. With each succeeding period of active treatment the ratio is materially lessened. After a loss of from 30 to 40 pounds a longer interval of several months or an entire season is arranged.

We should remember that fat is a normal constituent of the body, and that our object should never be to entirely rid the body of it, but only the excess. Neither is it possible to fit all people finally to the same mold. Experience indicates the degree to which a given individual may carry the treatment. A certain fairly definite point is always reached where further loss of weight necessitates a very great and unreasonable restricting of the diet and increase in the measures intended to augment the energy requirements. This point can be regarded as the normal weight for the given individual.

The obese themselves, not the obesity, are to be treated. In other words, it is not a simple condition of overweight in most cases, but a very complicated group of symptoms due to a generally disordered nutrition. Our aim should be to "restore the nutritive equilibrium." Unless this can be accomplished, the results will not be permanent or the vitality improved. In treating the obese we are dealing largely with unnatural habits which must be changed. The patient has formed the habit of eating the wrong things or in inordinate amounts; he is taking too little exercise or of the wrong kind. It is necessary, therefore, literally to reorganize the entire program of life.

Further, the variety of the causes underlying the obesity indicates that in the routine laid down every attention must be given to the individual. No set formula can possibly be applied to all cases alike. In the following pages, therefore, a rather general program will be outlined, to be modified and adapted to the individual cases as is necessary.

The question often arises if the patient can obtain better results at home or at a health resort where the entire attention is devoted to the treatment. The answer is, I believe, that in the majority of cases far better results can be obtained by the former method. Cures made at a sanatorium are carried on under conditions which are essentially un-

natural, and little is accomplished in effecting any radical change in the mode of life. Ordinarily the patient who carries out this régime in a health resort gives himself up entirely to strenuous out-of-door exercise (walking, mountain climbing, etc.), a restriction of diet amounting to starvation, and severe purging, and in the brief period of a few weeks brings about a very material loss of weight. Returning to his home he finds it impossible to continue the particular sanatorium régime and soon lapses into his former mode of life, with the result that the lost weight quickly returns. The cure has been too rapid and carried on under conditions and in an environment quite apart from his daily life. Von Noorden says:

"In regard to these courses of rapid reduction treatment, it is much more important, in order to obtain permanent and lasting results, to induce the patient to follow certain sensible rules at home and to persevere in the mode of life that is arranged to suit the peculiarities of each case and the external circumstances in which the patient happens to be living."

Since, as explained above, obesity is the result of an excess of food over that which is utilized for the body needs, the treatment must consist in the regulation of the diet and of those factors which determine the body's needs for energy. Of the two, the former is of far greater importance, yet the latter is essential. Either if used alone is ineffectual.

Dietetic Treatment

Before discussing the dietetic regulations, it will be well to consider briefly the essentials of several of the more important and best known systems of diet for obesity. All are based on essentially the same principle, namely, to diminish the caloric value of the diet so far as is consistent with the maintenance of nutrition and strength. The method by which this is accomplished through the reduction in the quantity of the different food constituents varies considerably. The quantity of fluids allowed also differs materially, but in nearly all the diet may be considered a "dry diet." Systematic exercise is prescribed with varying emphasis.

The Harvey-Banting Cure.—In 1863 a pamphlet appeared in London entitled: "A Letter on Corpulence Addressed to the Public," in which the author gives an account of his success in reducing his own weight through a system of dieting laid down by his physician, Dr. Harvey. For a period of twenty years Banting had tried in vain many methods, some of them violent, of reducing his excessive weight, but, having failed, sought the advice of Harvey, who suggested a diet very poor in fats and carbohydrates. Meat was allowed freely, and also water and claret. The diet is as follows:

Breakfast, 9 A. M.—Meat (mutton, beef, kidneys, broiled fish, bacon, or cold meats), 4 to 5 ounces. Tea without sugar or cream, 1 cup, 9 ounces. Toast (or 1 small biscuit), 1 ounce.

Dinner, 2 P. M.—Lean meat or fish, 5 to 6 ounces. Vegetables (any kind except potatoes, carrots, and parsnips). Dry toast, 1 ounce. Fruit (cooked, but unsugared). Claret, sherry, or Madiera, 2 to 3 glasses.

Tea, 6 P. M.—Fruit, 2 to 3 ounces. Rusk (or toast), 1 or 2. Tea without sugar or cream, 1 cup.

Supper, 9 P. M.—Lean meat or fish, 3 to 4 ounces. Claret or sherry, 1 to 2 glasses.

During the course of about ten months Banting lost 35 pounds, and was strikingly improved in general health. On the basis of his own experience, Banting speaks of the especial importance of the absolute restriction of all butter, bread, milk, beer, fat meats, and sugar.

The above diet represents roughly about 172 gm. proteins, 250 gm. fruit and vegetables, 90 gm. bread, and 1,020 c.c. fluids, or a total of probably about 1,200 calories. Its chief characteristics are, therefore, (1) abundance of protein; (2) very marked restriction of fats and carbohydrates; (3) water in normal amounts, and moderate quantities of light wines.

Although one of the most simple and popular of the many methods of treating corpulence, Banting's régime is really of very little value. The most serious objection lies in the undue predominance of the protein food, which in such quantities is difficult of digestion and assimilation, and is apt to lead to gastric and intestinal disorders, and, furthermore, puts undue demands on the kidneys. Likewise, the restriction of the fats and carbohydrates is entirely unreasonable and so great as to lead to a disturbance of nitrogenous equilibrium, it seems certain. The excess of nitrogenous food may be oxidized to supply energy, but less easily than carbohydrates and fats. The excess thus available for heat and muscular work is inadequate. The diet is also monotonous.

The Epstein Diet.—W. Epstein likewise tried a special form of diet on himself, with good results, which has since been extensively employed, particularly in Germany. The unsatisfactory results obtained by the use of Banting's diet led Epstein to formulate a plan which, in many respects, is the exact opposite. Epstein claims that his "cure" can be applied without serious interference with the ordinary manner of life of the average individual or undue self-denial. He further aims by his diet to produce lasting cure, instead of temporary results. The principles on which this form of treatment is based, as defined by its author, are as follows: It has been proved that the ingestion of moderate amounts of fat does not lead to an increase of body fat, and that a reduction of weight may be accomplished by a diet rich in fat, provided the carbo-

hydrates be limited and the mode of life made to conform to normal standards. Fat is a necessary constituent of normal diet, and cannot be excluded entirely without serious detriment to the organism. A diet rich in fat, according to Epstein, satisfies the hunger more completely and for a longer period than one composed chiefly of protein and carbohydrates. He denies that this is due either to resulting indigestion or depression of the appetite, as suggested by critics. The true explanation is found in the fact that fat remains in the stomach for a considerable period and, therefore, requires a proportionately large amount of work on the part of this organ.

In brief, this system of diet consists in: (1) a considerable limitation in the carbohydrates; and (2) a slight relative increase in the fat. Only such vegetables are proscribed as contain a high percentage of starch, the so-called green vegetables rich in water being allowed in abundance. A special form of bread containing from 20 to 30 per cent of albumin is recommended. Fruits, raw and stewed, without sugar, are allowed in moderation, likewise a small quantity of wine poor in sugar and alcohol. Beer is especially prohibited. Protein is given in somewhat restricted amounts. Fluids are not restricted, as in many other systems, but, according to Epstein, the large amount of fat definitely satiates the appetite for fluid and thus less is taken. Three meals a day are given:

6 to 7 A. M.—Tea without sugar or milk, 250 c.c. Dry toast, 50 gm. Butter, 20 to 30 gm.

2 P. M.—Thin soup. Fat meat with fat gravy, 130 to 180 gm. Green vegetables. Salad. Fresh fruit (apple or berries). Light Rhine wine, 2 to 3 glasses. Soon after this meal, plain, strong tea, 250 c.c.

7.30 to 8 P. M.—Meat with fat (egg or fish), 75 to 80 gm. White bread, 30 gm. Plenty of butter. Cheese (occasionally). Fresh fruit.

The value of the Epstein diet is usually given as protein, 102 gm.; carbohydrates, 47 gm.; and fat, 85 gm., or the equivalent of about 1,300 to 1,400 calories.

That the results attributed by Epstein to the increase in fat mentioned above actually follow is doubted by many. It is the opinion of von Noorden that the carbohydrates in considerable quantities are quite as effective as the fats in satiating hunger. Many patients cannot with comfort take a diet so rich in fat. The program laid down by Epstein is, however, one which can be very readily adapted to different individuals, and is especially applicable in those who are fond of fat foods.

The Oertel Cure.—The "Oertel cure" has enjoyed a wide popularity in Germany. This system of diet, to quote Oertel, "is based on the pathological changes in the heart and amount of circulatory changes

caused by them. To avoid burden to the heart we must diminish the quantity of both solids and fluids." He believes that large amounts of fluid seriously interfere with the involution of the body fat and, therefore, great stress is laid on the withdrawal of fluids. This he advises should be brought about by restricting the fluids taken and by depletion of the body tissues by sweating. In those with normal heart action the normal physiological measure of 1,500 c.c. per diem of fluid is allowed; in those with weak heart action, from 750 to 1,200 c.c. With very large individuals, or when the body temperature is high, the quantity is sometimes raised to 1,800 to 2,000 c.c. The diet is chosen with regard to the type of case, whether "plethoric," "anemic," or "hydremic." Protein is greatly increased, while the carbohydrates and fats are correspondingly cut down, the latter proportionately more than the former.

Oertel System of Diet

Diet	Albumin	Fat	Carbohydrates	Calories
Minimum	156	25	75	1,180
Maximum	170	45	120	1,608

The maximum diet is prescribed for those doing hard muscular work. A general daily menu is given:

Breakfast.—Wheat bread, 35 gm. Coffee, 120 gm., with milk, 30 gm., and sugar, 5 gm. 2 soft boiled eggs (or meat, 100 gm.), 90 gm. Butter, 12 gm.

Second breakfast.—Milk, Rhine wine, or bouillon (or water), 100 gm. Cold meat, 50 gm. Rye bread, 20 gm.

Dinner.—Broiled beef, 150 to 200 gm. Salad or vegetables, 50 gm. Cereal (or bread, 25 gm.), 100 gm. Fruit, 100 gm. Rhine wine, 250 gm.

Tea.—Coffee with milk, 30 gm., and sugar, 5 gm.

Supper.—Caviare (or smoked salmon, 18 gm., or 2 soft boiled eggs), 12 gm. Game, 150 gm. Cheese, 15 gm. Rye bread (or fruit, 100 gm.), 20 gm.

Careful consideration is given to exercises and baths.

The above method is, on the whole, one of the most satisfactory, and because of its flexibility can be adapted to the various types of cases. In the opinion of many authorities, the total protein is too high. Grave danger sometimes accompanies the restriction of fluids, and the majority of cases ordinarily seen do not furnish the definite indication in form of heart weakness as given by Oertel.

The Schweninger System.—The Schweninger system combines restriction of diet with exercise (gymnastics and massage). The diet differs but little from Oertel's. He gives somewhat more carbohydrates,

less fat, and the fluids are restricted only with meals or within one to two hours following:

7 A. M.—Mutton chop. Bread without butter.
8 A. M.—Cup tea with little sugar.
10.30 A. M.—Small slice bread and sausage.
12 M.—Soup, meat, potatoes, green vegetables, cheese, 2 glasses white wine, fruit.
4 P. M.—Cup tea with little sugar.
7 P. M.—Little bread with cheese.
9 P. M.—Cold meat, salad, 2 glasses wine.

Robin's Diet.—Robin contends that the ingestion of large amounts of fluid increases the oxidizing powers. The diet is ordered with reference to two classes into which he divides all cases of obesity according to the cause, namely, first, those resulting from increased assimilation, and, second, those resulting from decreased oxidation of food. In the first he reduces the fats and especially the fluids; in the second he gives large quantities of liquids in order to increase metabolism.

Robin's diet gives two good meals a day, and is characterized by being made up essentially of nitrogenous substances and green vegetables. He also gives careful directions regarding exercise and the general hygiene.

8 A. M.—1 egg. Bread, 19 gm. Meat, 20 gm. Cup weak tea without sugar.
10 A. M.—2 eggs. Rusk, 5 gm. Wine or water (or tea without sugar), 150 gm.
12 M.—Lean meat, 250 gm. Vegetables, 100 to 150 gm. Raw fruit, 100 to 150 gm. Red wine, 1 to 2 glasses.
7 P. M.—Meat, 100 gm. 1 egg. Vegetables, 150 gm. Cup weak tea without sugar.

Bouchard's Method.—Bouchard claims less weakening effects in the use of his method than are seen with many. His aim is the improvement of general nutrition as well as loss in weight. The diet consists exclusively of 1,250 gm. of milk and five eggs (1,200 calories) per diem, divided into five meals at four-hour intervals for a period of twenty days. Following this the patient is given a more varied diet, but without increasing the amount of proteins. The proper balance of the various food constituents is later maintained by a careful choice of green vegetables and fruit. The fats are given only in such small quantities as are necessary to take care of the bile and pancreatic juice. Much use is made of physical therapy.

Hirschfeld's Diet.—Hirschfeld's diet closely resembles Epstein's, but furnishes only about 45 gm. instead of 85 gm. of fat. It restricts all the

nutrients, especial emphasis being laid on the necessity for satisfying the appetite without increasing unduly the amount of nutrient.

Breakfast.—Cup black coffee and roll.
Forenoon.—2 eggs.
Dinner.—Bouillon with 30 gm. rice (weighed uncooked). Lean meat, 250 gm., with little fat.
Afternoon.—Black coffee.
Supper.—Cream cheese, 50 gm. Bread, 100 gm. Butter, 10 gm.

Von Noorden's System.—Von Noorden's system combines diet regulation with exercise and hydrotherapy. Particular attention in these regulations is given to the different grades of obesity and to the complications. For practical purposes von Noorden arranges three groups with regard to the severity of dietary restriction necessary. In the *first grade* the total calories are cut down about one-fifth, namely, from about 2,500 to 2,000 heat units, and the treatment continued for a long time. The monthly loss in weight at first should not be greater than from 3 to 4 pounds, and later not more than from 2 to 3 pounds. This moderate reduction in the food is sufficient only for those leading a life requiring a relatively great amount of muscular activity in the open air. In the *second grade* the diet is reduced approximately two-fifths, that is, from about 2,500 to 1,500 to 1,400 calories. Here also the rapidity of reduction in weight and the total loss will depend on the amount of energy used in exercises or work. As a rule, from 4 to 6 and later 2 to 4 pounds per month may be lost. The treatment may be continued practically without interruption for many months, or even years. It is especially adapted to those leading an indoor life, but who can continue treatment for a long time; to strong individuals who can be sent to the mountains and without medical supervision may combine the dieting with moderate travel; to those with complicating diseases, particularly of the heart, and, finally, to those cases of high-grade obesity with whom the ordinary diet is to alternate with periods of restriction. The reduction in the *third grade* is three-fifths, or from 2,500 to 1,400 to 1,000 calories, and corresponds roughly with the diets proposed by Banting, Oertel, Epstein, and others. It represents the most extreme reduction of the diet and should be employed with great caution. The loss in weight is usually from 6 to 12 pounds per month.

Von Noorden gives three chief meals with small lunches of low caloric value during the intervals:

8 A. M.—Cold lean meat, 80 gm. Bread, 25 gm. Cup tea or coffee (little milk, but no sugar).
10 A. M.—1 egg.
12 M.—Cup strong soup without fat.

1 P. M.—Small plate clear soup. Lean meat or fish, 150 gm. Potatoes, 100 gm. Green vegetables. Fresh fruit (or compote with sugar), 100 gm.

3 P. M.—Cup black coffee.

4 P. M.—Fresh fruit, 200 gm.

6 P. M.—Glass skimmed milk (or tea).

8 P. M.—Cold lean meat, 125 gm. Pickles, etc. Graham bread, 30 gm. Small serving cooked fruit (without sugar).

The value of this diet is given as, roughly: 156 gm. protein, 29 gm. fat, and 112 gm. carbohydrates, representing 1,366 calories. A glass of wine is permitted twice each day, but not with the principal meals. Von Noorden regulates the number of heat units in the diet according to the weight of the individual and the needs for energy, as indicated by the mode of life. No routine restriction of the fluids is made except as especially indicated by heart and other complications.

Karrell's Diet.—Karrell recommends an absolute milk diet in the treatment of obesity complicated with circulatory disorders, especially in the case of edema. The total amount per day in some instances among Karrell's cases was as low as 800 c.c. Exercise is kept at a minimum. Moritz reports the results of very careful metabolism experiments made with especial reference to this diet. He finds it especially valuable in cases with heart complications and nephritis. The total quantity given by this author is from 1,200 c.c. to 2,500 c.c. per diem, divided into small amounts, five to eight times daily. The precise amount is accurately regulated according to the body weight, as a rule from 16 to 17 calories per kg. of body weight being given. He recommends more exercise than Karrell. It is claimed for the "milk cure" that it acts as a diuretic, gives very prompt results, that it is most simple of regulation, and even in small amounts completely satisfies the appetite and thirst. As carried out by Karrell and Moritz, however, it is a more rigorous restriction than some patients can tolerate without more or less harmful effects. Many cannot take milk exclusively for a long period, and with the majority it soon becomes a very tiresome diet. Perhaps the most serious objection is the fact that sooner or later the patient must return to a mixed diet, and meantime nothing has been accomplished in the way of acquiring a knowledge or habit of regulation of the normal diet in order to control the body weight.

Comparison of Diets.—A comparison of the proportion of nutrients and fuel values of some of the more important of the above diets is given in the table on the following pages.

General Principles to Be Observed.—The reduction of weight in the obese, if done scientifically, is attended with no dangers whatsoever, but unreasonable or careless restrictions in the diet almost inevitably lead to

Comparison of Various Diets

Diet	Protein, Grams	Fat, Grams	Carbohydrates, Grams	Total Calories
Normal diet	100	150	350	3,240
Epstein	100	85	50	1,400
Harvey-Banting	172	8	81	1,100
Hirschfeld:				
Maximum	134	46	122	1,500
Minimum	95	43	106	1,220
Oertel:				
Maximum	170	45	120	1,608
Minimum	156	25	75	1,180
Robin	140	44	82	1,290
Von Noorden	155	28	112	1,366

unfavorable symptoms, or at times even to serious detriment to the general health. Reduction should, therefore, never be undertaken except under the close supervision of a competent physician. As has been emphasized above, the loss of superfluous adipose tissue is a matter which depends on much more complex regimen than the mere cutting down of the food ingested. All measures adopted should be employed to the end that the individual's mode of life be so reorganized that fat tissue is not only reduced, but the weight permanently maintained at the point reached. Of all the methods used, dietetic regulation is with very few exceptions the most important, yet others are essential. Success in treatment is attained only when the underlying causes of the obesity are sought out and treated.

The patient must be under constant surveillance, and to this end should be seen by the physician at least once each week, certainly during the first part of the treatment. Explicit directions regarding the kinds and exact amounts of food to be taken are necessary, and equally precise records of the food taken should be regularly furnished by the patient. By no other means is this possible except by a daily report of every article of food eaten, together with the approximate amount. In a few instances it may be necessary actually to weigh the food eaten, but under ordinary circumstances a sufficiently exact idea of the daily diet may be obtained if the quantity is given in terms of simple measure, that is, "one tablespoonful," "average slice," etc.

I have often found it helpful to have patients weigh the food for the first one or two weeks in order that they may be able to indicate accurately the quantity eaten. The value of the daily diet kept in this way can be figured with sufficient accuracy for all practical purposes.

An adequate safeguard against too great a reduction in the intake of food and at the same time more reliable than the total fuel value of the food alone is to be found in the observation of the weekly loss in

weight and the influence on the appetite, strength, and general appearance. After the first few weeks there should be little or no inconvenience from hunger, and both the strength and general appearance should improve with the loss in weight.

It is desirable that each case should have scales at hand in order that the weight may be taken daily. The variations from day to day and at different times of day are such that the weights, in order to be strictly comparable, should be taken on rising and without clothes. A chart of the weight by weeks is of great assistance to the physician in regulating the treatment.

It should be constantly kept in mind that eating is to some degree a matter of habit, and most people beyond early adult life eat to excess. A gradual cutting down of the amount of food ingested very promptly leads to a change in the habits, and the individual is completely satisfied with considerably less food.

The arrangement of meals is of some importance. The appetite is unquestionably satisfied more completely and the unpleasant sensations of hunger largely avoided by frequent meals, as suggested by von Noorden and others. Such an arrangement, however, is, as a rule, inconvenient, and, in my experience, entirely unnecessary as a routine. If during the long interval between the first two meals of the day there arise troublesome sensations of hunger or faintness, I advise a small luncheon at 11.30, consisting of a little fruit, a cup of bouillon, a glass of buttermilk or skimmed milk. In the afternoon a cup of tea and a very small amount of solid food usually suffice to allay these symptoms. The taking of fluid alone in some form without nourishment will frequently be sufficient.

It is well to take advantage of those factors which tend to depress the appetite to a moderate degree and to shun those which stimulate it. Prolonged chewing of the food reduces the appetite by causing satisfaction with a smaller volume of food, and should always be advised. Similarly, more food is generally eaten when the variety is great. For this reason relatively few courses are to be recommended, that is, seldom more than three to five. On the other hand, too monotonous a diet may depress the appetite unduly and should, therefore, be guarded against. Condiments and stimulants in general are prohibited, as they quicken the desire for food.

Physiological research as well as experience has proved that adipose tissue may be formed from any of the food constituents when taken in excess, as stated above, though from the proteins only to a relatively small extent. When the diet contains more protein than is utilized by the body for tissue repair, the superfluous portion is much more apt to be metabolized to form heat and energy. It follows, then, that under ordinary conditions the chief sources of body fat are the carbohydrates and fats. The question as to which serves the more important source

of fat has not been satisfactorily answered, but it seems probable that the carbohydrates are relatively more important in this direction than the fats.

Considering these facts, the fundamental principle may be laid down, in the dietetic treatment of the obese, that the first consideration is that the total number of calories per diem should be materially lessened rather than any particular restriction of special kinds of food be made. This principle is borne out in actual experience by the success attending the use of the different methods previously described, which differ greatly in the restrictions which they make with regard to the various food constituents. The total food value of the diet must be reduced considerably below that which is required by the system, and the difference between this value and that required is made up by oxidation of the organism's own fat. The degree to which this reduction should be made varies with each individual, and it is impossible to lay down any definite rule.

In the majority of instances I have found it necessary to reduce the caloric value at least one-half and sometimes two-thirds. For the average individual of normal health and reasonable activity, a diet consisting of 100 gm. protein, 60 gm. fat, and 120 gm. carbohydrates, or with a total caloric value of 1,448, may be considered a fair average. This represents, in the case of an individual weighing 200 pounds, approximately 16 calories per kg. of body weight in contrast to the normal average of 40 calories per kg. Some individuals will lose satisfactorily on a diet furnishing 1,800 or even 2,000 calories per diem, but, as a rule, in order to effect a loss of from 1 to 2 pounds per week, it is necessary to restrict the diet to about 1,400 calories. In a few instances I have employed a diet as low as from 900 to 1,000 calories. The reason for this marked reduction in the food is found in the relatively enormous fuel value of the body fat. For example, the oxidation of 2 pounds of body fat in a given week furnishes considerably more than 8,000 calories, or approximately 1,200 heat units per day.

While, as stated above, the cutting down of the caloric value of the food is the first essential, it is also very important that the diet be so selected as to avoid excessive hunger. The aim should be the satisfaction and not the satiation of the appetite, and this end is dependent to a very large degree on the volume of the food. In other words, one should choose a bulky or so-called "fodder diet." In order to accomplish this purpose it becomes necessary to restrict greatly those foods which for a given bulk have a comparatively high value. From the fact that 100 gm. of butter, for example, furnish 795 calories and 100 gm. of string beans, cooked, 21 calories, the force of the above principle is evident. It will be seen that the exclusion of even a moderate amount of butter will materially lower the fuel value of the diet, while the inclusion of an ordinary helping of string beans will furnish considerable bulk without the addition of

many calories. In general the types of food yielding a relatively large number of calories are almost exclusively the carbohydrates and fats; consequently these are the types of food which should be particularly limited. The degree to which each should participate in the restriction will depend largely on the taste of the individual. For those who are especially fond of carbohydrates I am accustomed to make the fats share more largely in the reduction, and vice versa.

In my experience the following menu fulfills the above requirements very satisfactorily:

Breakfast.—Cup black coffee (with milk, but no cream or sugar). Raw fruit (1 orange, apple, pear, or ½ grapefruit). Eggs (1 or 2, boiled or poached). Toast (1 or 2 small slices, that is, 10 to 20 gm., usually without butter).

11.30 A. M.—Cup bouillon (250 c.c. skimmed milk or buttermilk or fruit).

Luncheon.—Clear soup, 120 c.c. Moderately lean meat or fish, 100 gm. (or eggs). Two varieties green vegetables, 50 to 100 gm. each. Raw fruits.

5 P. M.—Tea without cream or sugar. (Small slice toast, 10 gm.)

Dinner.—Raw oysters. Moderately lean meat or fish, 100 to 150 gm. Two varieties green vegetables, 50 to 100 gm. each. Salad (fruit or vegetable) with small quantity of French dressing. Raw or unsweetened cooked fruit. Demi-tasse black coffee.

The above menu represents, according to the choice, a maximum and minimum value as follows:

Maximum and Minimum Value

Diet	Protein	Fat	Carbohydrates	Calories
Minimum	60	50	70	1,000
Maximum	100	70	165	1,738

Foods Allowed—*Meats and Fish.*—All lean meats and fish, except as noted below, but without rich dressings or sauce.

Thin soups.—In moderation.

Eggs.—In any form, except scrambled, fried, and omelette.

Fruits.—All fresh varieties (except bananas), and berries (without cream and sugar); cooked, if with saccharin.

Vegetables.—String beans, water cress, lettuce, radish, cucumber, asparagus, green peas, Brussels sprouts, cabbage, cauliflower, okra, onions, celery, watermelon, tomato, artichoke, spinach, white potato in moderation, mushrooms, squash, beets, turnips, carrots, parsnips, oyster plant, vegetable marrow (cooked with but little butter and no cream).

Miscellaneous.—Tea, coffee, skimmed milk, lemonade (with saccharin), ginger ale. Desserts made of gelatin, or Irish moss, if with but little sugar; use saccharin or saxin in place of sugar.

Foods to Be Avoided or Greatly Restricted—*Starches.*—Bread, crackers, cereals, macaroni, vermicelli, spaghetti, sago, tapioca, cornstarch, sweet potatoes, shelled beans, dried peas or beans, corn, and nuts.

Sweets.—Sugar, candy, dried fruits, syrups, fruit preserves, honey, marmalade, and sugar sauces.

Meats.—Pork, bacon, goose, sausage, croquettes.

Fish.—Shad, fresh salmon, eels, sardines, mackerel, bluefish. Fried fish.

Fats.—Butter, cream, olive oil, bacon, lard; fat meats and fishes.

Desserts.—Ices, rich puddings, cake, and gingerbread.

Miscellaneous.—Chocolate, alcoholic beverages, except claret and Rhine wine, thick soups, milk, cheese, pickles, and condiments.

Reference to the above lists will give a general idea of the choice of food, and to the following table more exact facts regarding the weights and relative values of those from which to select the diet:

PREPARED FOODS—EDIBLE PORTION *

Foodstuffs	Quantity	Weight Grams	Proteins		Fats		Carbohydrates		Total Calories	Calories per 100 Grams
			Grams	Calories	Grams	Calories	Grams	Calories		
1. MEATS										
Beef										
Corned beef, canned	1 slice	50	13.15	53.9	9.35	87.0	...	...	141	282
Roast	1 slice	100	22.30	91.4	28.60	266.0	...	...	357	357
Roast, very lean	1 slice	100	23.33	95.7	1.66	15.4	...	...	111	111
Steak, round, fat removed	1 slice	100	27.60	113.2	7.70	71.6	...	...	185	185
Steak, tenderloin	1 slice	100	23.50	96.4	20.40	189.7	...	...	286	286
Sweetbread	1 slice	80	32.00	131.2	.45	4.2	...	...	169	169
Tongue, canned	1 slice	25	4.88	20.0	5.80	53.9	...	...	74	295
Chicken										
Capon	1 slice	100	27.00	110.7	11.50	107.0	...	...	218	218
Fricasseed	1 slice	100	17.60	72.2	11.50	107.0	2.40	9.8	189	189
Roast	1 slice	100	32.10	131.6	4.40	40.9	2.10	8.6	181	181
Lamb										
Chop with bone	1 chop	100	21.70	89.0	29.90	278.1	...	...	367	367
Roast	1 slice	75	14.78	60.6	9.53	88.6	...	...	150	150

* From Food Values, 1911, Table II, by E. A. Locke, D. Appleton & Co.
Unless otherwise stated the values are for food as prepared for the table.
Abbreviations: a. = average, d. = diameter, h. = heaping, m. = medium, dsp. = dessertspoon, tbsp. = tablespoon, tsp. = teaspoon.

PREPARED FOODS—EDIBLE PORTION—*Continued*

Foodstuffs	Quantity	Weight Grams	Proteins		Fats		Carbohydrates		Total Calories	Calories per 100 Grams
			Grams	Calories	Grams	Calories	Grams	Calories		
1. MEATS—(Cont.)										
Mutton										
Boiled, lean	1 slice	75	23.18	95.0	3.38	31.4	...	...	126	168
Chop, lean	1 chop	100	22.60	92.7	4.50	41.9	...	...	135	135
Roast leg	1 slice	75	18.75	76.9	16.95	157.6	...	...	234	313
Pork										
Chop	1 chop	70	17.92	73.5	4.20	39.1	...	...	113	161
Ham, smoked, boiled as purchased	1 slice	33	7.29	29.9	6.80	63.2	...	...	93	291
Turkey										
Roast	1 slice	100	27.80	114.0	18.40	171.1	...	...	285	285
Veal										
Cutlet	1 cutlet	80	22.82	93.6	1.14	10.6	...	...	104	133
Roast	1 slice	75	21.33	87.5	1.00	9.3	...	...	97	132
2. FISH										
Bluefish	.....	100	25.90	106.2	4.50	41.9	...	...	148	148
Cod	.....	100	21.68	88.9	.27	2.5	1.58	6.5	98	98
Haddock	.....	100	21.98	90.1	.36	3.3	3.63	14.9	108	108
Halibut	.....	100	20.35	83.4	4.04	37.6	...	...	121	121
Mackerel	.....	70	11.73	48.1	4.84	45.0	2.62	10.7	104	148
Smelts	1 fish	14	2.23	9.1	.26	2.4	.06	.2	12	85
Spanish mackerel, broiled	.....	100	21.80	89.4	5.90	54.9	...	...	144	144
Sturgeon, Russian caviare	1 h. tsp.	10	3.00	12.3	1.97	18.3	.76	3.1	34	337
Trout, brook	.....	50	10.57	43.3	1.17	10.9	.62	2.5	57	114
Shellfish										
Clams, long	6 clams	150	12.90	52.9	1.5	14.0	3.00	12.3	79	53
Clams, round	6 clams	100	6.50	26.7	.4	3.7	4.20	17.2	47	47
Crabs, hard shelled, as purchased	1 crab	245	19.36	79.4	2.21	20.6	1.47	6.0	106	91
Lobster	.....	105	17.22	70.6	1.89	17.6	.42	1.7	90	86
Oysters	6 oysters	85	5.27	21.6	1.02	9.5	3.15	12.9	44	52
Oyster stew	4 oz.	124	6.07	24.9	11.06	102.9	10.53	43.2	171	138
3. SOUPS										
Beef, home-made	4 oz.	120	5.28	21.6	.48	4.5	1.32	5.4	32	26
Bouillon, canned	4 oz.	120	2.64	10.8	.12	1.1	.24	1.0	13	11
Consommé, canned	4 oz.	120	3.00	12.3	...	...	.48	2.0	14	12
Julienne, canned	4 oz.	120	3.24	13.3	...	...	.60	2.5	16	13
Tomato, canned	4 oz.	120	2.16	8.9	1.32	12.3	6.72	27.6	49	41
Vegetable, canned	4 oz.	120	3.48	14.3	...	...	.60	2.5	17	14

PREPARED FOODS—EDIBLE PORTION—*Continued*

Foodstuffs	Quantity	Weight Grams	Proteins		Fats		Carbohydrates		Total Calories	Calories per 100 Grams
			Grams	Calories	Grams	Calories	Grams	Calories		
4. DAIRY PRODUCTS AND EGGS										
Butter	1 ball	15	.15	.6	12.75	118.6	...	...	119	795
Cream										
"Average"	1 tbsp.	20	.74	3.0	5.14	47.8	.71	2.9	54	269
Cheese										
Camembert	1 h. tsp.	20	4.20	17.2	4.34	40.4	...	...	58	290
Dutch	2 scoops	20	7.42	30.4	3.54	32.9	...	...	63	316
Fromage de Brie	1 cu. in.	20	3.18	13.0	4.20	39.1	.28	1.2	53	267
Limburger	1 cu. in.	20	4.60	18.9	5.88	54.7	.08	.3	74	369
Neuchatel	1 cu. in.	20	3.74	15.3	5.48	51.0	.30	1.2	68	337
Roquefort	1 cu. in.	20	4.52	18.5	5.90	54.9	.36	1.5	75	375
Milk										
Buttermilk	1 glass	218	6.54	26.8	1.09	10.1	10.46	42.9	80	36
Koumiss	wineglass	130	3.64	14.9	2.73	25.4	7.02	28.7	69	53
Skimmed milk	1 glass	222	7.55	31.0	.67	6.2	11.32	46.4	84	37
Whole milk	1 glass	220	7.26	29.8	8.80	81.8	11.00	45.1	157	72
Whey	1 glass	203	2.03	8.3	.61	5.7	10.15	41.6	56	28
Eggs										
Hen's, boiled	1 egg	50	6.60	27.1	6.00	55.8	...	...	83	169
Hen's, uncooked	1 egg	50	6.70	27.5	5.25	48.8	...	...	76	159
Hen's, whites, boiled	1 egg	32	4.16	17.1	.06	.6	...	...	18	55
Hens', yolks, boiled	1 egg	18	2.89	11.8	5.99	55.7	...	...	68	376
5. VEGETABLES										
Artichokes, French	1 artichoke	360	6.48	26.6	.29	2.7	16.56	67.9	97	27
Asparagus, canned		125	1.88	7.7	.13	1.2	3.50	14.4	23	19
Beans:										
Butter	4 h. tbsp.	80	3.78	15.5	.24	2.2	11.60	47.6	65	81
String	2 h. tbsp.	60	.48	2.0	.66	6.1	1.14	4.7	13	21
Beets	2 h. tbsp.	70	1.61	6.6	.07	.7	5.18	21.2	29	41
Beet greens	2 h. tbsp.	100	2.20	9.0	3.40	31.6	3.20	13.1	54	54
Cabbage	3 h. tbsp.	100	.60	2.5	.10	.9	.40	1.6	5	5
Carrots	3 h. tbsp.	100	.53	2.2	.17	1.6	3.39	13.9	18	18
Cauliflower	2 h. tbsp.	120	1.08	4.4	.12	1.1	.48	2.0	8	7
Celery, uncooked	3 small stalks	55	.50	2.1	.05	.5	1.43	5.9	8	19
Cucumber, uncooked	8 thin slices	50	.40	1.6	.10	.9	1.55	6.4	9	18
Dandelion greens	2 h. tbsp.	100	2.39	9.8	1.01	9.4	10.67	43.8	63	63

PREPARED FOODS—EDIBLE PORTION—*Continued*

Foodstuffs	Quantity	Weight Grams	Proteins		Fats		Carbohydrates		Total Calories	Calories per 100 Grams
			Grams	Calories	Grams	Calories	Grams	Calories		
5. VEGETABLES (Cont.)										
Mushrooms, uncooked	2 large	45	1.58	6.5	.18	1.7	3.06	12.5	21	46
Onions	1 onion	100	1.20	4.9	1.80	16.7	4.90	20.1	42	42
Parsnips	4 slices	100	.22	.9	.29	2.7	1.46	6.0	10	10
Potatoes, boiled	1 medium	150	3.75	15.4	.15	1.4	31.35	128.5	145	97
Squash	2 h. tbsp.	100	1.36	5.6	.82	7.6	13.60	55.8	69	69
Spinach	2 h. tbsp.	100	2.10	8.6	4.10	38.1	2.60	10.7	57	57
Tomatoes, canned	2 h. tbsp.	70	.84	3.4	.14	1.3	2.80	1.4	16	23
Tomatoes, uncooked	m. size	200	2.40	9.8	.40	3.7	8.00	32.8	46	23
Turnips	2 h. tbsp.	140	.45	1.8	.08	.7	.91	3.7	6	4
6. FRUITS										
Fresh, as purchased										
Apple	a. size	150	.45	1.8	.45	4.2	16.20	66.4	72	49
Blackberries	3 h. tbsp.	100	1.30	5.3	1.00	9.3	10.90	44.7	59	59
Cantaloupe	½ melon	465	1.40	5.7	...	...	21.39	87.7	93	20
Cherries	about ¼ lb.	100	.90	3.7	.80	7.4	15.90	65.2	76	76
Cranberries	1 cup	100	.40	1.6	.60	5.6	9.90	40.6	47	47
Currants	4 h. tbsp.	100	150	6.2	...	...	12.80	52.5	59	59
Grapefruit	½ large	300	2.37	9.7	.60	5.6	30.27	124.1	139	46
Grapes	1 bunch	150	1.50	6.2	1.80	16.7	21.60	88.6	112	74
Gooseberries	4 h. tbsp.	90	.90	3.7	...	...	11.79	48.3	52	56
Huckleberries	4 h. tbsp.	100	.60	2.5	.60	5.6	16.60	68.1	76	76
Lemon	a. size	130	.91	3.7	.65	6.0	7.67	31.4	41	32
Orange	a. size	250	1.50	6.2	.25	2.3	21.25	87.1	96	37
Peach	a. size	128	.64	2.6	.13	1.2	9.86	40.4	44	34
Pear	a. size	156	.78	3.2	.62	5.8	19.81	81.2	90	57
Pineapple, edible portion	2 slices	100	.40	1.6	.30	2.8	9.70	39.8	44	44
Plum	a. size	35	.32	1.3	...	...	6.69	27.4	29	81
Raspberries	3 h. tbsp.	82	.82	3.4	...	...	10.33	42.3	46	56
Strawberries	4 h. tbsp.	100	1.00	4.1	.60	5.6	7.40	30.3	40	40
Watermelon	large slice	300	.60	2.5	.30	2.8	8.10	33.2	39	13
7. BREAD, CRACKERS, ETC.										
Bread										
Toasted	4x2x¼ in.	10	1.15	4.7	.16	1.5	6.12	25.1	31	313
White, homemade	3x4x½ in.	37	3.37	13.8	.59	5.5	19.72	80.9	0	270
Crackers										
Butter	d. 2 in.	4	.38	1.6	.40	3.7	2.86	11.7	17	427
Graham	3 in. sq.	8	.80	3.3	.75	7.0	5.90	24.2	34	429

PREPARED FOODS—EDIBLE PORTION—*Continued*

Foodstuffs	Quantity	Weight Grams	Proteins		Fats		Carbohydrates		Total Calories	Calories per 100 Grams
			Grams	Calories	Grams	Calories	Grams	Calories		
Crackers—(Cont.)										
Pretzels	6	6	.58	2.4	.23	2.1	4.37	17.9	22	375
Saltines	2 in. sq.	3	.32	1.3	.38	3.5	2.06	8.4	13	492
Soda:										
Educators	2 in. sq.	3	.97	4.0	...	...	1.39	5.7	10	333
Uneeda biscuits	3 in. sq.	6	.59	2.4	.55	5.1	4.38	17.7	25	424
8. MISCELLANEOUS										
French dressing	1 dsp.	11	...	...	8.00	74.4	...	...	74	673
9. NON-ALCOHOLIC BEVERAGES										
Coffee or tea with ¼ cup milk	1 cup	246	2.06	8.4	2.50	23.3	3.12	12.8	45	18
Lemonades										
Egg lemonade with 1 egg, 2 tbsp. lemon juice	1 large glass	314	6.70	27.5	5.25	48.8	2.35	9.6	86	27
Lemonade with white of egg, 2 tbsp. lemon juice	1 large glass	297	4.10	16.8	.08	.7	2.35	9.6	27	9
Plain lemonade with 2 tbsp. lemon juice	1 glass	264	...	...	...	...	2.35	9.6	10	4

Except at breakfast, where it is usually wise to allow a cup of coffee, the limitation of fluids in all forms at meals is advisable. It seems questionable if they have any significant effect on metabolism, but when taken with solid food, fluids certainly tend to increase the quantity eaten. For this reason, and because they stimulate the appetite directly, soups are best excluded from a strict diet. An abundant quantity of fluid should be taken at other times, however, best at least two hours after, or not later than one-half hour before meals. Bedtime and on rising are also favorable times for free drinking of fluids. The frequent observation of the specific gravity and quantity of the urine furnishes a sufficiently reliable guide as to the amount of fluid necessary. As a rule, 1,500 to 2,000 c.c. of water or its equivalent in any form of liquid during twenty-four hours is sufficient, but this standard varies within wide limits, depending on the size of the individual, the type of life, the presence or absence of certain complicating diseases, season of the year, and many other factors. Rarely, if ever, should the total fluids be reduced lower than 1,000 c.c. per diem. The abundant consumption of liquids is especially indicated in those cases

taking a large amount of protein food, in order to aid in the excretion of the products of nitrogenous metabolism.

Alcohol when oxidized in the body yields a relatively large number of calories, and even in small amounts may add sufficient value to the diet to prevent satisfactory loss in weight. These alcoholic beverages with a high content of alcohol or carbohydrates should under nearly all conditions be strictly forbidden. An exception is found in those patients who have habitually taken such beverages to excess, and in these it is best to permit a moderate quantity. If the weight is decreasing satisfactorily an occasional glass of claret or Rhine wine can be taken at dinner without interfering with the success of the treatment.

Many patients suffer great deprivation from the restriction of the starchy foods, and especially bread. In such cases the substitution of bread made from gluten flour or one of the many proprietary breads poor in starch will often be found helpful.

Mechanical Therapy

Though of less value than the dietetic treatment, the employment of methods to increase the demands for energy with resulting increased oxidation of food is indispensable. This end is reached through many channels, and the choice of the particular method and the degree to which it shall be used depend on many considerations. The production of either heat or muscular work means the oxidation of fat and carbohydrates in the food, and, if these sources be inadequate, the body fat as well, and, therefore, acts advantageously in the reduction of weight. A further and still more important reason for the carrying out of this form of treatment is the beneficial influence which exercise exerts on the general vitality, and especially on the muscular system.[1] The oxidation of fat is always most active, and consequently the loss in weight most rapid in those whose general condition of health is most nearly normal. It follows, then, that, in the well-developed and vigorous obese, methods of physical treatment serve chiefly to increase the metabolism of fats and carbohydrates, while in the case of the debilitated the first consideration is the development of the body vitality through improvement in the functions of the internal organs. Careful employment of these methods makes it possible to bring about satisfactory results with less rigid restriction of the diet.

Whatever the method used may be, the most careful attention must be given to the general health of the patient, especially to the condition of the circulatory system and kidneys. In case serious disorders of these organs be present, great harm may be done by their injudicious use. The same applies to nearly all other complicating conditions. In some instances it may be wise at first to use only dietetic treatment. The response

[1] Notably that of the heart.—Editor.

to physical treatment varies in almost inverse ratio to the age; in those past middle life and in the aged the results are, as a rule, very unsatisfactory and often entirely negative.

Von Noorden has emphasized the fact that physical therapy gives the best result in those individuals in whom the obesity is due to the "retarded metabolism" rather than dietetic errors. As in the case of the dietetic treatment, constant care should be given to the minutest measures, for, if too strenuous or if the weight reduction be too rapid, there is always danger of loss of body albumin as well as of the body fat, with resulting loss of vigor. For short periods only it may at times be advisable to use vigorous methods, but in general the rule may be laid down to begin with mild procedures, and to increase gradually as the condition of the patient and the response to treatment warrant. The observation of the effects on the patient is a far safer guide than any a priori estimation of how much can reasonably be given.

Exercise.—Exercise is the most convenient of the physical measures used, and in the cases without complications the most effective. In the great majority of instances this form alone is sufficient. The influence of exercise in augmenting the metabolism is largely effected through stimulation of circulation, hence the special danger in the presence of circulatory disorders, particularly high-grade atheroma or cardiac insufficiency. Since the majority of obese subjects, either as a cause or a result of the condition, take comparatively little bodily exercise, it is almost always necessary to prescribe a definite graduated program. One occasionally sees cases, however, even among the corpulent, of undue physical exertion, most frequently perhaps among those who in the effort to reduce their weight have resorted to very severe forms of physical exercise. Any form which is so severe as to be in the slightest degree exhausting leads, as a rule, if continued, to a depression of the general vitality. Cases of failure to reduce weight due to too much exercise are not uncommon. Because of this danger, it is my practice to discourage the participation in the most vigorous types of sports where the excitement of sharp competition leads to unconscious excess in muscular exertion. Oertel especially has advocated systematic walking, graded as to time, rate, and degree of incline. While useful in cases of weak heart, such a precise regulation in the average case is entirely unnecessary. Only general supervision of the actual exercise is, in the great majority of instances, all that is required. Preferably it should be in the open air and the particular kind is a matter of indifference. I select that form which is most pleasant and easiest for the particular patient, whether it be walking, riding, climbing, competitive sports, provided they are not too vigorous, swimming, etc. Naturally the great majority take up walking, and, as a rule, can very soon work up to a walk of three-quarters to an hour each morning, and for a shorter period of time in the afternoon. For the average case this is sufficient, but in those with

unusual vigor more is sometimes indicated. Deep breathing during the exercise contributes to its beneficial results.

Three factors, then, are to be considered in regulating the form and degree of exercise: (1) the general strength and vitality of the individual, and especially of the heart; (2) complicating conditions; and (3) individual habits and preferences.

Nearly every system of reduction cure gives some place to *calisthenics,* and, undoubtedly, if conscientiously followed out, they are an aid. Few persons in my experience have the persistency to carry them out with sufficient regularity to produce results. Where possible, it is wise to insist on a few of the more vigorous movements for a few minutes on rising and at bed time.

Passive mechanical exercise, as with the Zander apparatus, and resistance movements afford a means of some importance, but it is seldom possible to employ them with cases treated in their homes. These have the great advantage that they can be absolutely controlled, and are mainly used in those cases of obesity with heart and other complications in which active exercise is contra-indicated. They are especially in vogue in the health resorts.

Massage.—In my hands massage has very frequently proved an important adjunct to the general treatment, though of far less value than active exercise, and, when the latter can be satisfactorily taken, unnecessary. Through its action in stimulating the circulation and restoring the tone of the depleted muscles, it exerts a considerable influence on metabolism. To some degree local accumulation of fat can be effectively treated by massage. In women of very sedentary habits it is of great assistance. It is necessary that it should be very vigorous and done regularly at practically daily intervals.

Hydrotherapy

Rubner found after a cold bath at 15° C. for fifteen minutes a decomposition of only 10.7 gm. of fat, which was increased to 19.7 gm. with cooling off and after effects, and calculated that a loss of 1 kg. would require 100 such baths. Although in general the results of hydrotherapy appear comparatively slight, when taken in conjunction with exercise the benefits cannot be questioned. Strasser considers the various hydrotherapeutic measures of some value, but chiefly important as preparatory to massage. Von Noorden gives five indications for the use of hydrotherapy in the treatment of obesity, as follows: (1) to improve the condition of the skin; (2) to harden against colds and bronchitis; (3) to increase the resistance of the nervous system; (4) to improve circulation; and (5) to accelerate the loss of weight. Through these results hydrotherapeutic measures undoubtedly exert a very marked influence in building up the

general vitality and stimulating metabolism. Because of this indirect influence of procedures of this sort, they must be regarded as of some real value in the program for the reduction of the obese. The more special measures can only be given in a specially equipped institution, but such simple measures as cold baths may be carried out at home very satisfactorily.

Medicinal Treatment

This form of treatment is, on the whole, both unsatisfactory and unnecessary. Careful regulation of the diet and exercise with possibly the addition of massage and hydrotherapy are sufficient to reduce satisfactorily the great majority of cases. The treatment of obesity is essentially better hygiene. Of the many drugs suggested, the majority have no noteworthy action and should be uniformly discarded. Various iodin preparations at one time or another have enjoyed a considerable reputation as fat reducers, but no convincing proof has yet appeared of any especially favorable action, and no indications are present for their use.

A large number of secret internal remedies and external applications have been much advertised and are widely used by the laity. Hutchison gives the analyses of a considerable number of these nostra. This report of his examinations gives no basis for their use. In the treatment of various complications, such as disorders of circulation and digestion, drugs may, of course, find an important place in treatment. Their indications and method of administration need not be discussed here.

Extracts of certain glandular organs have long been known to exert a very marked influence on metabolism. Most important among these are the preparations made from the thyroid, which, probably through stimulation of the nervous system, lead to an enormous stimulation of the metabolic processes. Thyroid extract has been so widely employed in reduction cures as to merit more than passing mention. Yorke-Davies, Wendelstadt, and Magnus-Levy have shown that the administration of the thyroid gland in the obese leads to an increase of the oxygen consumption and carbon dioxid excretion. Somewhat later work on animals by Voit proved the important fact that the increased metabolism following this method of treatment resulted in an increased oxidation of body protein. Von Noorden believes this to be a sufficient contra-indication to its use in reducing corpulency, and further states that the results mentioned above, while the rule, do not in all cases necessarily follow. He also lays stress on the fact that in obesity the thyroid secretion is diminished.

Hoyten studied 100 cases of obesity, and concludes that the action of thyroid extract in the young is nil, while the maximum results are obtained in adult females between the ages of thirty-five and forty-five. The last-mentioned author, together with many others, speaks warmly of the excellent effects obtained by the use of thyroid preparations. In the majority

of cases large doses unquestionably lead to unfavorable or even alarming symptoms, among them glycosuria, or true diabetes mellitus, vertigo, insomnia, digestive disturbances, palpitation, tachycardia, arythmia, and, rarely, to Graves' disease. It is also true that the stimulation of metabolism is purely an artificial one, and therefore in no way affects permanently the body weight. If used, it should be given in small doses of 1 to 2 gr. twice or three times daily, and very cautiously increased.

In a few instances, in middle-aged women especially, I have observed excellent results follow the employment of this method as supplementary to the dietetic-mechanical treatment. As a rule, it is unnecessary, and should not be given, except in those rare cases where a strict regulation of diet and exercise fail to bring about a loss in weight. Good results in women, especially those past the menopause, have been recorded, but the method lacks a scientific basis and is of very doubtful value.

Gerhardt, Seuz, and others report good results from the use of sodium borate in doses of from .25 to .5 gm. (gr. iv to viii) three times daily, in conjunction with a dietetic regimen. Seuz in his series of 6 cases met with severe gastro-intestinal symptoms in several. In general this method does not commend itself.

Many of the health resorts both in this country and Europe are well known for their treatment of obesity. The most frequented are: Marienbad, Wiesbaden, Homburg, Carlsbad, Ems, Tarasp, Kissingen, Vichy, and Virginia Hot Springs. The content of mineral salts in these waters is somewhat varied both in kind and amount. Nearly all excite increased peristaltic action of the bowels, leading to frequent evacuations. The obvious result of the purging is to prevent assimilation of food and inevitable depression of nutrition if continued. It is clear that such a method should be used with the greatest caution, and for only very short periods, lest general weakness, especially of the circulation, result. Anemia complicating corpulence is an absolute contra-indication to the purging treatment. The plethoric type, on the other hand, do well under such measures, if not too vigorously pushed.

For the average case of obesity without serious complications treatment in a health resort is not to be recommended. The loss in weight is brought about under conditions which are largely artificial, and the results are frequently only temporary, since the treatment has not been directed to the end that the habits of life be altered. As a rule, the rate of loss in weight is unreasonably rapid. It cannot be denied that most excellent results are obtained in the health resorts, but it is impossible to separate the effects of the alkaline waters from other methods of diet, exercise, massage, and hydrotherapy, with which they are combined.

It is well in the majority of cases to supplement the dietetic-mechanical treatment by the use of mild cathartic mineral waters in some form. In fact, it often happens that in the beginning of treatment the restriction of

certain foods leads to a marked diminution in the bulk of the residue in the intestines and resulting obstipation. This annoying condition can generally be overcome by the regulation of the fruits and green vegetables in the diet, but it is often necessary to give cathartics at least for a time.

Treatment after Reduction

In the majority of cases the permanency of the results obtained depends almost solely on the faithfulness with which the regimen which brought about the loss in weight is continued. When the point is reached at which no further loss is desired, the total calories in the food may be materially increased without any significant gain in weight resulting, but the additional diet must be chosen with some care. The treatment, if properly carried out, has by the time the reduction of weight has taken place led to a more or less complete change in the mode of life with reference to the diet and exercise. The patient should, without great self-denial, be able to abstain permanently from the articles of food which have a particularly high fuel value. With occasional supervision on the part of the physician the patient soon learns by daily observations of the weight to regulate the choice of the kinds and amount of food to maintain the weight at a chosen level. Several hundred calories must be added to the daily diet to prevent further reduction, and this will ordinarily suffice to satisfy the appetite, and I have frequently observed an increase of from 800 to 1,000 heat units without any gain in weight. Likewise, a moderate degree of regular exercise must be systematically followed, though considerably less than during active treatment will suffice.

REFERENCES

Bergmann, von. Ztschr. f. exper. Path. u. Therap., 646, 1909.
Bischoff. Quoted by Hauser, Méd. mod., Paris, xvi, 17, 1905.
Bouchard. Maladies par le ralentissement de la nutrition, 118, Paris, 1882.
Epstein. Die Fettleibigkeit und ihre Behandlung, 1882.
Gerhardt. Therapie der Gegenwart, iv, 240, 1902.
Hirschfeld. Ztschr. f. klin. Med., xxii, 142, 1893.
Hoyten. Brit. Med. Journ., ii, 197, 1906.
Hutchison. Ibid., xxiv, 150, 1907.
Karrell. Edinb. Med. Journ., xii, 97, 1866.
Lusk. Science of Nutrition, 66, 72, 109, 1906.
Magnus-Levy. Berl. klin. Wchnschr., xxx, 650, 1895.
Moritz. München. med. Wchnschr., lv, 1569, 1908.

Noorden, von. Metabolism and Prac. Med., iii, 693, 704, 1907.
——— Nothnagel's Spec. Path. u. Therap., vii, 143, 1900.
Oertel. 20th Century Practice, ii, 625, 1895.
Robin. Bull. gén. de thérap., 133, 1897.
Rubner. Ztschr. f. Biol., xxi, 356.
Schweninger, S., and Buzzi. Sammlung med. Abhand., No. 4, 1894.
Seuz. Therap. d. Gegenw., 158, 1903.
Strasser. Marcuse u. Strasser, Physical. Therap., xvi, 34, 1906.
Voit. Ztschr. f. Biol., xxxv, 116, 1897.
Wendelstadt. Deutsche med. Wchnschr., l, 934, 1894.
Yorke-Davies. Brit. Med. Journ., xlii, 158, 1894.

CHAPTER XXIV

METABOLIC DISEASES

T. B. Futcher, George Blumer, and F. Forchheimer

ALKAPTONURIA AND OCHRONOSIS

T. B. Futcher

This remarkable and very rare urinary anomaly was first described by Bödeker in 1859. There have been only some 50 to 60 cases reported in the literature up to the present time. To the substance which produces the striking urinary findings Bödeker gave the name "alkapton," owing to the property possessed by urine containing it of rapidly absorbing oxygen from the air in the presence of an alkali. It was not until 1891 that Baumann and Wolkow first demonstrated that the peculiar reactions of alkaptonuria are due to the presence of homogentisic acid, which is the dioxyphenylacetic acid derived from hydrochinon. This observation has been amply confirmed in the subsequent cases reported.

The characteristics of the urine are briefly as follows: When voided it usually has a normal appearance, but rapidly acquires a deep brown color and ultimately becomes black on exposure to the air. The brown color is greatly hastened and intensified by the addition of an alkali, its development being accompanied by absorption of oxygen from the air. The urine is of normal specific gravity. It reduces alkaline copper sulphate solutions with the aid of heat, the mixture at first being of an inky black color. Ammoniacal silver nitrate solutions are reduced in the cold. It does not reduce alkaline solutions of bismuth. The urine does not ferment with yeast and is optically inactive. The addition of ferric chlorid solution produces a transitory bluish green color. Diapers and linen of affected children turn a deep brown color on exposure to the air.

The anomaly is congenital, persists throughout life, and does not impair the health. It predominates in males. Of the first 40 cases reported up to 1902, A. E. Garrod found 29 were males and 11 females. Clinically,

the condition is important owing to the possibility of its being mistaken for diabetes mellitus, on account of the urine reducing alkaline copper solutions. This mistake had occurred in the case reported by the writer in 1898. The patient was one of two brothers manifesting both alkaptonuria and ochronosis and later reported by Osler. The association with ochronosis, or ochre-colored pigmentation of the cartilages, described by Virchow in 1866, was first pointed out by Albrecht in 1902. Although all cases of ochronosis are not accompanied by alkaptonuria, C. P. Howard found the two associated in 24 reported cases. In the cases of ochronosis associated with alkaptonuria it is believed that the homogentisic acid in some way favors the deposition of melanin in the cartilages. Theoretically, according to Abderhalden and Guggenheim, a ferment, tyrosinase, is believed to act on the oxyphenyl group of the homogentisic acid molecule favoring the production and deposition of melanin.

Alkaptonuria is due to a disturbance of the intermediary metabolism of proteins. The usual destruction of the aromatic protein cleavage products, tyrosin and phenylalanin, appears to be interfered with. When tyrosin and phenylalanin are fed to a normal individual they are completely burned up. When they are administered to an alkaptonuric there follows an increased amount of homogentisic acid in the urine. The healthy individual readily burns up ingested homogentisic acid while in the alkaptonuric it is excreted unchanged. There is believed to be a disturbance of the katabolism of the amino-acids in such a way that the final cleavage of the benzene ring represented in homogentisic acid is no longer possible.

Garrod's investigations have thrown an interesting light on this anomaly. He brought out two points. There is a familial tendency. Of 40 cases collected, 19 occurred in 9 families. He also showed that a number of cases were in children of parents who were first cousins but who did not themselves manifest the peculiarity. In this respect, he points out that alkaptonuria resembles albinism and possibly also cystinuria.

Treatment.—There is no treatment that has any influence on the condition. The anomaly does not seem to affect the health. Where alkaptonuria is found, careful examination of the cartilages of the ears, knuckles, ribs, etc., should be made to see whether there is an associated ochronosis.

LITHURIA

By T. B. Futcher

The term "lithuria" is rarely used to-day and might well be abandoned. One might suppose that it dealt essentially with an excess of lithium in the urine, which, however, is not its true significance. It is

possible that the term may have a Greek derivation signifying "stone in the urine." At all events, "lithic acid" and "uric acid" had become practically synonymous to the older writers, and "lithuria" is the name used to designate those cases where a deposit of amorphous urates and uric acid crystals appears more or less persistently in the urine.

Uric acid, in combination, exists normally in the circulating blood to the amount of 1 to 3 or 4 mg. per 100 c.c. of blood. It is eliminated in the urine in combination chiefly with sodium and ammonium and to a smaller extent with potassium, calcium and lithium. The salts of uric acid may be precipitated out of the urine under various circumstances in an amorphous form, often causing a very abundant sediment. The color varies from a pale yellow tint, due to urochrome, to a deep pink, due to combined uroerythrin. The uric acid may become separated from its bases and crystallizes out in rhombs or prisms, which are usually of a deep red color owing to contained urinary pigments. The crystals resemble granules of Cayenne pepper.

The occurrence of a marked precipitate of urates or uric acid crystals in the urine does not by any means necessarily indicate that there is an excess of uric acid in the blood or even in the urine itself. There are various factors which favor the precipitation of uric acid salts from the urine. Roberts mentions the following: (1) high acidity; (2) poverty in mineral salts; (3) low pigmentation; and (4) high percentage of uric acid. High acidity probably plays an important part. Klemperer finds that a deficiency of the pigment, urochrome, has an important influence in favoring the deposition of uric acid.

The amount of uric acid eliminated in the urine daily by the normal adult on a general mixed diet is from 0.4 to 1 gm., the average, according to Hammarsten, being 0.75 gm. If the kidneys are functioning normally, the amount of uric acid eliminated is diminished on a purin-free diet and materially increased by feeding foods rich in purins, such as sweetbreads, kidneys, liver, brains, etc. The point to be emphasized, however, is that we must draw no definite conclusions as to whether there is an increased output of uric acid in the urine from the amount of urates and uric acid crystals precipitated. The only way to determine the amount of uric acid excretion is to save and measure the urine carefully for each twenty-four hours and make quantitative determinations of the uric acid by one of the recognized methods. Naturally the character of the diet should be carefully taken into consideration at the same time.

The presence of an abundant sediment of urates or uric acid crystals should not be used as a diagnostic indication of the actual existence of gout. In the most marked cases of chronic tophaceous gout there is, between acute attacks, a diminution of uric acid elimination in the urine and no uric acid sediment of any kind occurs. At the height of and for a day or two after an acute gouty attack there is often an increased output

of uric acid even above the normal and a sediment may occur in the urine. Members of gouty families occasionally have renal calculi of uric acid origin or may pass uric acid gravel. These members are often spared the arthritic manifestations.

The urine of the normal individual when allowed to stand in cold weather not infrequently shows a precipitation of urates. Much more abundant is the precipitation of urates in the concentrated urines of febrile patients. The urate sediments are often a source of considerable anxiety to the neurasthenic patient until his mind has been relieved on the subject. In leukemia, especially in the myeloid form, there is often an increased output of uric acid, and the latter may be thrown out in crystalline form.

Treatment.—With regard to therapy, the dietetic management is important in those cases where urates and uric acid deposits occur in the urine of individuals with proved gout. Foods rich in purins, especially sweetbreads, kidneys and liver, should be excluded and even meats, chicken and fish should be eliminated or reduced to a minimum. Tea and coffee should be banned. A purin-free diet consisting of milk, eggs, fruits, green vegetables and farinaceous foods should be prescribed. The patient should drink very freely of water. Alkalis, such as the citrate or acetate of potash, given freely with water, may be helpful. The much-heralded urinary solvents that appear from time to time soon run their course and are forgotten. Water remains our best uric acid solvent.

INDICANURIA

T. B. Futcher

One of the products of bacterial putrefaction of proteids in the intestine is indol, the others being skatol, phenol, cresol, etc. The indol is absorbed from the intestine, oxidized in the body to indoxyl, conjugated in the liver with sulphuric acid, and eventually excreted in the urine as indoxyl sulphate of potassium. It is, therefore, as indoxyl sulphate that the so-called urinary pigment "indican" is excreted in the urine. It is not found in the urine of the newborn child and not until cow's milk is given. These facts point towards the supposed influence of bacterial action on proteids in the intestine. It is normally present in adults on a mixed diet up to 5 to 25 mg. in the twenty-four hours. The output is greater on a meat than on a vegetable diet. In pathological states the total daily excretion may reach from 50 to 150 mg. Indoxyl sulphate may be markedly increased without a corresponding marked increase of the total ethereal sulphates, that is, sulphuric acid combined with the aromatic alcohols, skatoxyl, phenol, cresol, in addition to indoxyl. The total

ethereal sulphates, on the other hand, may be increased without an increase of the indoxyl sulphate alone.

In a general way indoxyl sulphate is increased in those conditions accompanied by rapid decomposition of proteid in the intestinal tract. It is increased in impaired intestinal peristalsis due to peritonitis and ileus. Its production seems to depend on the presence of trypsin. In paresis of the small intestine, whether from peritonitis or obstruction, the output of indoxyl sulphate shows a marked and rapid increase. In paresis of the colon, on the contrary, there is either no increase or one which begins late. It is increased in intussusception and in obstruction of the small intestine due to new growths or twists. Chronic constipation may cause an increased output but this is far from constant. There is an increase also in cholera infantum, typhoid and in some cases of nephritis.

There is evidence that an increased elimination of indoxyl sulphate is not alone confined to decomposition of proteid in the intestines. It probably occurs wherever there is decomposition of albumin in the body. Thus there is an increase in gangrene of the lung, fetid empyema, putrid bronchitis, and in advanced pulmonary and intestinal tuberculosis.

There is a diminished output in obstruction of the pancreatic duct, which seems to bear out the belief that the presence of trypsin is necessary for the eventual formation of indoxyl sulphate. It is increased in hypochlorhydria and gastric anacidity. Senator found an increased output in chlorosis. Gastric anacidity may explain the increase found in pernicious anemia. Indigo calculi have been described.

The urine in indicanuria usually appears normal when voided. Instances have been recorded in which the indoxyl sulphate has become broken up in the body, and a bluish color of the urine has been noted on voiding. Occasionally an alkaline urine containing an increased amount of indoxyl sulphate may exhibit a bluish film on the surface.

In testing the urine for indoxyl sulphate a perfectly fresh specimen should be examined, as the salt breaks up readily and fallacious results may be obtained. The demonstration of indoxyl in the urine and its quantitative determination depend on its oxidation to indigo blue. The simplest qualitative test is that of Obermayer. The urine is cleared of disturbing substances by precipitating them out with one-fifth its volume of 20 per cent acetate of lead and then filtering. An equal amount of fuming hydrochloric acid containing a little ferric chlorid (4 c.c. of ferric chlorid to 1,000 c.c. of hydrochloric acid) is then added. In a few minutes the blue color appears, and may be taken up by adding chloroform and gently shaking. Jaffé's test may also be used. For the quantitative estimation of indoxyl sulphate and of the total ethereal sulphates the proper works must be consulted.

While the presence of an increased output of indoxyl sulphate is of

interest as an indication of increased proteid decomposition in the body, particularly in the intestines, and much has been published on the subject in the last two decades, too much importance has been attached to the whole question. An increased output may be of some value in diagnosis in obscure abdominal conditions. There is too great a tendency, however, to interpret an increased output as a manifestation of that bugbear of the profession "intestinal auto-intoxication," the "scrap basket" into which too many abnormal states are cast without proper effort being made to find the fundamental cause of the ailment elsewhere.

Treatment.—From what has been said, it will be readily appreciated that "indicanuria" is a manifestation, in the majority of cases, of proteid putrefactive changes in the intestinal tract or elsewhere in the body. The treatment, therefore, must be directed toward ascertaining the primary cause and relieving it if possible. In the intestinal group, if there are no conclusive evidences of obstructive features, a judicious use of saline laxatives may be helpful. The various lactic acid bacilli preparations have been much lauded where there has been a persistent increase in the indoxyl output, but Barr, in 32 such cases, failed to get any beneficial results.

PENTOSURIA

T. B. Futcher

Glucose, the sugar in the urine of patients with diabetes mellitus, is a hexose. Only in recent years has it been known that pentose, a sugar with five carbon atoms in a chain, may in rare instances be persistently excreted in the urine, irrespective of what the diet may be.

Three distinct types of pentosuria have been described and the distinction between them is important:

1. Alimentary pentosuria, analogous with alimentary glycosuria, occurs whenever large amounts of vegetables or fruits containing pentosans are eaten. Since the power of the organism to destroy such sugars is much less than in the case of the hexoses, they not infrequently are excreted in appreciable quantities after the eating of certain fruits, such as plums and cherries, when beer is freely used, and when considerable quantities of prepared fruit juices are taken. The distinguishing feature about this pentose, however, is that it is optically active, no optically inactive vegetable pentose being known.

2. In rare cases of severe diabetes the inability of the organism to burn the ordinary carbohydrates extends to the pentoses and glycosuria is accompanied by pentosuria.

3. The third group comprises the cases of chronic or essential pentosuria. These cases, occurring without any relationship to the ingested pentoses and persisting without alteration for years, present an interesting problem in intermediary metabolism. It is with these that we are particularly concerned.

Essential Pentosuria.—In 1892, Salkowski and Jastrowitz first observed the excretion in the urine of an optically inactive sugar, which did not ferment with yeast, and which they identified as a pentose by the melting point of its osazone. The condition is rare. In 1906, when Theodore Janeway reported 2 cases in brothers, only 17 cases had been reported. These, with 2 other unpublished cases, 1 observed by von Jacksch and another by Dunham, made a total of 21 cases up to that date.

The sugar excreted in the urine of essential pentosuria is the optically inactive r-arabinose. This is the only known occurrence of an optically inactive sugar anywhere in nature. It may be recalled here that in the vegetable kingdom the most important pentoses are l-arabinose and l-xylose. In the animal body, pentoses are present in the nucleoproteids, that of the pancreas and liver having been identified as l-xylose. These pentoses are optically active, however.

The percentage of pentose in the urine is usually low. Blumenthal's case with 1 per cent is the highest. This author, with Bial, has found the r-arabinose in the blood. The quantity of urine is never excessive. The specific gravity is moderately increased, and the acidity is said to be high. The power to burn dextrose has been normal in all the cases in which tolerance tests have been made. The total amount of the pentose eliminated daily is practically constant, although Janeway and Klercker found a somewhat diminished excretion on a milk or purin-free diet. The latter observer found a certain parallelism between the total nitrogen and pentose in the urine, which has suggested some relation between the abnormal production of r-arabinose and the activity of metabolic processes.

A family predisposition apparently exists, 19 cases occurring in 14 families. Garrod says Jews are predisposed. The condition persists throughout life so far as is known. The health of the individual is not impaired, although in a number of the cases neurasthenic symptoms and neuralgic pains have been prominent. Others have been perfectly well when released from the restrictions of a diabetic regimen.

The true nature of the malady is still unknown. It is an anomaly of intermediary metabolism. Garrod speaks of it as a "sport" of metabolism analogous to alkaptonuria and cystinuria.

The proper diagnosis of the condition is generally led up to by the finding of an atypical reaction with Fehling's solution. Pentosuria should be suspected if the urine reduces Fehling's solution in an atypical way, the color remaining unchanged for a minute or so after boiling and then

suddenly turning a greenish yellow or muddy orange throughout. Such a reaction should lead to confirmatory tests. If the urine yields good crystals with the ordinary phenylhydrazin test, does not ferment with yeast, and is optically inactive, pentosuria is probably present. The diagnosis is clinched by finding that the urine gives a positive orcin test and by determining that the melting point of the osazone in performing the phenylhydrazin test is found to be between 156° and 160° C. The details of performing these tests can be found in any standard work on Clinical Diagnosis.

The chief significance of these cases is that they are likely to be mistaken and treated for diabetes mellitus, unless the practitioner constantly watches out for and appreciates the significance of atypical Fehling's reactions, and takes the precaution to utilize other tests. Some, as in one of Janeway's patients, have been turned down for life insurance.

Treatment.—Apparently there is no particular treatment, dietetic or otherwise, that seems to affect the condition. The anomaly apparently persists throughout life and is a condition *sui generis*. It seems to be a type of an alternate intermediary metabolism. Although the amount of pentose eliminated is practically constant on any diet, Janeway and Klercker think that a liberal milk diet is favorable, and Blumenthal advises a moderate restriction of meats. Those cases, previously mistaken for diabetes mellitus, should be released from the dietetic restrictions of the latter disease.

OXALURIA

F. Forchheimer

For many years a so-called oxalic acid diathesis was accepted; indeed, is still accepted. While oxalates are found in the urine in certain combinations of symptoms, it by no means follows that they cause the symptoms. If we look at the origin of oxalic acid and its salts we find that various views exist: one, in which the substance is supposed to be exogenic; the other, in which it is considered endogenic; and a third, in which both are considered as playing a rôle. It is probable that the latter view is correct. The greater part of the oxalic acid is derived from the food, the lesser from metabolic changes which have not been definitely settled. It is claimed by some that in the endogenous form oxalates are the result of albuminous metabolism, by others of changes in the carbohydrate group. Whichever it may be, it is certain that the oxlates can be reduced most readily by excluding foods which contain much oxalic acid.

The combination of symptoms which were supposed to be due to oxaluria are those of chronic intestinal intoxication: symptoms on the part of the gastro-intestinal tract, the nervous system, the urinary organs.

Physical examination reveals the changes in the intestine which are found in chronic intestinal auto-intoxication. The urinalysis shows increase in the indican, with or without increase of the aromatic sulphates, and of calcium oxalate crystals, all found with more or less regularity in chronic intestinal auto-intoxication. When we study the question from this point of view, it is not likely that the origin of the symptoms is due to the oxalates. Moreover, all the symptoms which are ascribed to oxaluria are found in chronic auto-intoxication of the intestinal type, without the presence of oxalates in the urine. It seems more than likely, then, that we have confused the effects with the cause, and when oxaluria per se requires treatment its correct treatment is that of chronic intestinal auto-intoxication.

It is especially the local effect of the so-called oxalic diathesis which requires treatment. The urinary evidences of this condition are the constant presence of blood in the urine in microscopic or macroscopic quantities, and of calcium oxalate crystals, which affect the patient generally as the result of hematuria or locally by irritating the urinary passages or producing calculi. It is for these reasons that oxaluria requires especial therapeutic mention. The first problem is to reduce the quantity in the urine. For this purpose it is necessary to restrict the diet in such a way that oxalic acid is not introduced into the economy. It must not, however, be done with the idea that oxalates can be removed entirely from the urine, because, as has been stated before, the oxalates are metabolic end-products.

The first measure to be enforced is *diet,* which must not include articles which are known to contain large quantities of calcium oxalate: rhubarb, tomatoes, pineapple, apples, sorrel, strawberries, and lemons should be eaten sparingly or refrained from altogether in the beginning of the treatment. It is impossible to prevent the introduction of oxalate of lime, as it is found in practically all vegetables. Excess in eating should be forbidden. The stomach should be treated; it is an accepted fact that there is a connection between oxalic acid formation and dyspepsia, usually due to subacidity. Much good may be done, in this condition, by the internal administration of mineral acids: dilute hydrochloric or dilute nitrohydrochloric acids (0.6 to 0.1 c.c., m. xv), given well diluted and after meals. As oxalic acid is formed from uric acid, the treatment of gout may be applied with advantage in many instances in which there is a history of gout. In those cases which are of the dyspeptic or gouty type, which, as a rule, if not always, is due to chronic intestinal auto-intoxication, cures such as are conducted in Carlsbad and in places having sulphur waters are valuable and successful.

PHOSPHATURIA

F. Forchheimer

The origin of the phosphoric acid in the urine is from two sources: it is exogenous or endogenous. By far the larger amount comes from the food, and for our present purpose need not be considered. This is the case except in neurotic subjects who watch their urine and are guided in their feelings by the presence or absence of its phosphatic precipitate. In these patients it is well to explain to them how the amount of the phosphates is determined, and that their test is of no value whatsoever as the precipitation of the phosphates in the urine depends upon many factors. Endogenously phosphoric acid is formed from organic combinations which are specially found in the nervous system: nuclein, glycerophosphoric and oleophosphoric acids, lecithin, and protagon. Under these circumstances it is not strange that the purin bodies are usually increased in this form of phosphaturia.

Under all circumstances the diagnosis of phosphaturia should only be made after qualitative and quantitative analyses are done, otherwise the subject becomes one of those general terms which cover over poor diagnoses and do much harm. When the diagnosis has been properly made, much can be done by treatment. It is necessary that patients who present too much phosphoric acid in the urine, followed by disturbances that can be attributed to it, should be treated. The diet should be arranged so that albumin is taken in minimum quantities, carbohydrates making up the deficit in calories. Moreover, vegetable albumin and milk may be given. In the purely endogenous form diet does not seem very valuable. The general condition, reduction in wear and tear, curtailment or abstinence from work, should be recommended. In these cases the treatment applied to all reduced neurotics should be applied, as to food, rest, and general measures.

It has been shown by von Noorden and his school that the administration of calcium carbonate prevents the phosphates from being eliminated by the urine. Elimination takes place under these circumstances into the bowels at all times, and at least one-half and more of the phosphates can be prevented from leaving the system by the kidneys. Creta preparata (gm. 1 to 2—gr. xv to xxx) is given twice or three times a day. There is no difficulty in verifying this statement, and, in as far as preventing the development of local conditions in the kidneys and bladder is concerned, this measure may be valuable. As a rule, however, more is gained by preventing the formation of phosphates than by removing them.

HEMOCHROMATOSIS

George Blumer

Nature and Etiology.—The exact nature of this disease is still in doubt, but it is placed among the metabolic diseases rather than the diseases of the blood-forming organs because there is no evidence of blood destruction and definite evidence of disturbance of pigment elimination which is probably due to chemical rather than mechanical causes.

The disease is a chronic one which occurs almost exclusively in males of middle age. It is characterized pathologically by the deposition of iron-bearing and iron-free pigments in the tissues and organs of the body, particularly the liver, pancreas and skin, and the formation of scar tissue as a result of cell degeneration following the pigmentary deposit.

Symptoms.—Clinically the completely developed disease is characterized by pigmentation of the skin, cirrhosis of the liver, and hyperglycemia with or without glycosuria. In atypical cases one or more of these features may be absent. Skin pigmentation is present in about 80 per cent of patients with this disease. It is most marked on the exposed parts, the axillæ and the genitalia and varies in color from a yellow to an ashen gray. It is patchy at times and grayish discoloration of the gums may accompany it. The hepatic cirrhosis is usually well marked, the size of the liver depending on the acuity of the process. Usually the liver is enlarged and, as a rule, the spleen is secondarily swollen from chronic passive congestion. The diabetes, which may be a late manifestation, is generally of a rather severe type.

Treatment.—There is no known treatment of the underlying pigmentary changes unless Mallory's hypothesis that it is associated with chronic copper poisoning can be shown to be true of human hemochromatosis. If this should be the case, prevention would consist in legislative enactments forbidding the use of copper salts in canned foods and in drinks and also making the use of copper stills for the production of distilled liquors illegal.

The treatment of the developed disease is that of cirrhosis of the liver or diabetes or both. If cirrhosis appears early, omentopexy would seem desirable but this, of course, would afford no relief to the lack of pancreatic hormone and the treatment for this is the same as for any other case of diabetes.

REFERENCES

Oxaluria

F. Forchheimer

Mackenzie, Hector. Journ. Am. Med. Ass., 5, 1907.

Hemochromatosis

George Blumer

Blanton and Healy. Arch. Int. Med., xxvii, 406, 1921.
Dunn. Brit. Med. Journ., ii, 783, 1921.
Mallory, Parker, and Nye. Journ. Med. Research, xlii, 461, 1920-1921.
Telling. Brit. Med. Journ. ii, 784, 1921.

DISEASES OF THE DIGESTIVE SYSTEM

CHAPTER XXV

DISEASES OF THE MOUTH

Otto H. Foerster

A thorough investigation of the oral cavity should be a routine procedure in the general examination of patients at all ages. It is of importance not only for the detection of diseases peculiar to the mucous membranes or limited to the oral cavity, but also for the aid it may provide in the recognition of obscure general morbid conditions. The distorted scar on the soft palate or pharyngeal wall, the perforation of the hard palate, or the leukoplakic and sclerotic tongue, furnish indisputable evidence of an old syphilitic infection, and their detection, as the result of an examination of the oral cavity, may lead to the proper interpretation of an obscure vascular, hepatic or other visceral condition. Gingivitis and rapidly developing ulcerative stomatitis are often among the first signs of acute leukemia; bleeding, soft, and bluish gums should direct attention to the possible presence of scurvy; scars on the tongue may indicate epilepsy, and the detection of a blue line along the gums will reveal an intoxication by lead. Furthermore, carious, filled or crowned teeth and diseased tonsillar tissue are recognized to-day as frequent sources of systemic infection, and the knowledge of this alone sufficiently indicates the value and importance of a careful examination of the mouth.

This comprises inspection in a good light, that is not too intense, of the lips, buccal mucosa, palate, gums, teeth, tongue, floor of the mouth, faucial regions, pharyngeal mucosa, and salivary glands, often aided by palpation, with careful attention to the various recesses. Plates and removable bridgework should be removed so that the underlying parts may be included in the examination. Note is made of the color and consistency of the mucosa, of deposits on its surface, of congested or injected areas, scars and cicatricial deformities, fistulous tracts, pigmentations, eruptive lesions, localized infiltrations, tender, painful or anesthetic areas, and of other departures from the normal.

It may be desirable in special instances to test the sense of taste or to examine the saliva as to its reaction and chemical composition. From

studies made by Hench and Aldrich it appears that the saliva also may serve to reveal the urea content of the blood and thereby afford a valuable index of renal functional capacity. In addition, bacteriological investigation is indicated when the presence of diphtheria, gonorrhea, tuberculosis, or other specific condition is suspected.

Under normal conditions the mouth harbors many bacteria, the majority of which are harmless saprophytes, though there are some that are capable of developing pathogenic properties when the conditions are favorable. The bacteria are mainly derived from without through the medium of food, drink, and the inspired air; but when parts that communicate directly or indirectly with the oral cavity are involved in infective processes, the bacteria may gain access to the mouth from within the body. An example of this is observed in pulmonary and laryngeal tuberculosis in which tubercle bacilli are conveyed to the mouth in the sputum.

The number and variety of microörganisms is largely dependent upon the attention given to mouth hygiene, and when this is neglected an increase in the bacterial flora follows. Bacillus maximus, Streptococcus brevis, and Leptothrix innominata are species of bacteria commonly found in the mouth, as are also the fusiform bacillus of Vincent, Micrococcus catarrhalis, and several varieties of spirochetes. A number of microörganisms which may be the pathogenic agents in focal infections are often present in the mouth, and are of the staphylococcus, streptococcus, pneumococcus, and fusiform bacillus types. Other varieties that have been found in the mouth include the gonococcus, Bacillus pyocyaneus, Friedländer's bacillus, the bacilli of diphtheria, tuberculosis, tetanus, and leprosy, and the Spirochæta pallida. Several of these, as the pneumococcus, streptococcus, Bacillus pyocyaneus, fusiform bacillus, and the diphtheria bacillus, are sometimes found in the mouths of healthy persons. Fungi also may invade the oral cavity. The Oïdium albicans found in thrush, and Leptothrix buccalis, which forms plugs in the tonsillar crypts, are familiar examples. Monilia candida appeared to be the causative agent in a severe infection of the oral mucosa ending in carcinoma, described by Engman and Weiss.[1]

SYSTEMIC INFECTION OF ORAL ORIGIN

Recent studies have developed a new and greater significance of the conception of systemic disease arising from localized foci of infection, in which oral sepsis occupies a prominent place. Infected teeth and tonsils, and some forms of stomatitis, through the infective agents concerned in the process, or their toxins, may be the sources of origin for

[1] Certain forms of amebæ, usually harmless but at times pathogenic (Flexner), may also be found in the mouth.—Editor.

pathologic changes in distant parts of the body. It is highly probable that some instances of ulcerative endocarditis and cryptogenetic sepsis originate in conditions of oral sepsis, and Rosenow and Meisser have asserted the existence of an etiologic relation between infected teeth and renal calculus. Injury to the mouth by dental instruments appeared to be the primary source in several instances of pemphigus observed by Ormsby. In a patient with pemphigus, under the care of the writer, the disease developed immediately following a localized Vincent's infection of the gingival mucosa attributed to dental injury. The importance of oral sepsis as a causal factor in pernicious anemia, as maintained by William Hunter, awaits further confirmation.

Prevention and Treatment.—From the foregoing it is evident that oral sepsis is a distinct menace to the health of the individual and demands corrective measures. Far too little attention has been given to the condition of the mouth by medical men and, as a rule, the field has been tacitly left to the care of the dentist. Preventive measures are to be instituted early in life, and should concern themselves with proper nutrition during infancy and childhood, the establishment of proper habits of oral hygiene, observation as to the condition of the lymphoid structures, and with the periodic inspection of the teeth and gums by the dentist. Corrective measures may require attention to dental caries, the extraction of teeth or of old root fragments, the removal of pathologic tonsillar and adenoid tissues, and the treatment of abscesses or other suppurative conditions.

DISEASES OF THE LIPS

Cheilitis Exfoliativa.—This is a chronic desquamative inflammation of the lips, characterized by the formation of small, dry, adherent scales or scalelike crusts, which exfoliate in thin, micalike flakes, exposing an underlying glazed, dry, or fissured surface. In severe cases heavy crusts may be formed. It is generally confined to the vermilion border of the lower lip, but may involve both lips, or the upper lip alone, and in exceptional instances may extend to neighboring parts of the skin and buccal mucosa, and rarely to the tip of the tongue. There is an entire absence of the bright red, thickened, exudative condition observed in eczema. The disorder tends to persist for months or years, with occasional periods of exacerbation and improvement, and is usually kept aggravated by chewing of the lip and attempts at premature removal of the scales.

The *etiology* is unknown, though the condition may be related to seborrheic dermatitis which is often found associated with it on the face and scalp. The histopathology is that of an inflammatory process, with parakeratotic changes and acanthosis.

Treatment.—The disease resists treatment and tends to recur. The teeth and mouth must be kept clean, and pungent or irritating mouth washes should be avoided. The alkaline antiseptic solution (N. F.) may be used well diluted. Fissures are not to be cauterized by nitrate of silver or other agents, but their opposing sides may be held in contact by zinc oxid adhesive tape renewed twice a day, whereupon they will heal spontaneously (Pusey). A soft, 5 per cent sulphur ointment, an ointment containing 2 per cent salicylic acid and 25 per cent naftalan, or a 5 to 10 per cent resorcin lotion, used alone or conjointly, are often of benefit. Repeated applications of carbon dioxid snow in crayon form with moderate pressure have proved successful. Unfiltered Roentgen-rays in ⅛ to ¼ skin unit dose (MacKee and Remer scale) applied weekly for six doses, and exposure to radium have been employed with success. The lesions of an associated seborrheic dermatitis should likewise be given remedial attention.

Cheilitis Glandularis Apostematosa (Myxadenitis Labialis).—This is a chronic inflammation of one or both lips, usually the lower only, with swelling and edema, enlargement of the mucous glands, and dilatation of the follicular orifices throughout the vermilion border. The hypertrophied mucous glands and ducts are felt as nodules beneath the labial mucosa, and a yellowish, glistening, thin mucoid secretion can be readily expressed through the dilated orifices. Abscess formation is an unusual complication. An active catarrhal inflammation of the gingival, buccal, and pharyngeal mucosa is often an associated condition, and the turbinates and the lymphoid tissues of the throat and nasopharynx are frequently found to be hypertrophied.

The *etiology* is obscure, but significance may attach to the frequent association of the disorder with the catarrhal inflammation and lymphoid hyperplasia already mentioned. Sutton found an increase in the amount of glandular tissue, dilatation and thickening of the ducts of the mucous glands, and only slight changes in the corium. He considers the condition congenital in origin and a manifestation of an excessive supply of glandular tissue to the nose, pharynx, mouth, and lips.

Treatment.—The disorder, though persistent, is benign in character. In several cases there was a beneficial response to potassium iodid given during a period of one or two months. The Roentgen rays employed as in cheilitis exfoliativa may be of value. Sutton has found the most satisfactory method of treatment to be excision of the individual lesions by means of a small cutaneous punch.

Retention Cysts of the Mucous Membrane of the Lip.—These are usually located in the lower lip opposite the left cuspid tooth, are nearly always single, and may reach the size of a large pea. They contain an opalescent, ropy fluid, and after incision promptly refill. The cysts are

due to dilatation of one or more of the ducts of the labial glands (Sutton).

Treatment.—Excision or the application of the actual cautery to the interior of the cyst are the preferable procedures in treatment. The application of caustics is generally followed by recurrence.

Eczema.—Eczema of the vermilion surface of the lips is often an extension of eczema of the cutaneous border. The lips are swollen and thickened, scarlet or dull red in color, and desquamate in thin flakes or may develop vesicles and pustules over a part or the entire vermilion surface, with crusts and painful fissures. The disorder is persistent, and is maintained by the movements of the lips and by wetting of the parts with saliva.

Treatment.—In every patient the possibility that the disorder is an "artificial eczema" due to irritant mouth washes (formalin), dentrifices, cosmetics, and perfumes, must be carefully investigated at the outset. If this diagnosis is established the avoidance of the irritant and the application of zinc oxid ointment or emulsion are sufficient rapidly to relieve the condition. In the absence of such chemical causation, the condition of the mouth should be investigated and appropriate treatment or hygiene instituted when necessary. The use of tobacco in any form must be forbidden, and highly spiced or salty foods should be avoided. In acute stages the lips may be covered with compresses dipped in an alkaline or colloid solution, followed by a soothing ointment, such as 10 to 15 per cent naftalan in a soft paste of zinc oxid, starch, and petrolatum, or combined with zinc oxid ointment. In some cases an emulsion of equal parts of limewater and olive oil is more serviceable. When the inflammation is less acute, an ointment containing 2 or 3 per cent of ammoniated mercury may be used to stimulate absorption of the inflammatory products. Still later a protective application for the vermilion surface will be found useful; this is made by adding enough white wax to simple ointment to produce a stiff mixture. In chronic cases with thickening, small doses (⅛ skin unit) of Roentgen rays given weekly are indicated.

Perléche.—Perléche is a contagious, inflammatory disorder of the labial commissures, usually bilateral, in which the mucous membrane is thickened, wrinkled, whitish and macerated, and often transversely fissured. The disorder may extend to the inner surface of the lips and to the adjacent skin, or for a short distance along the vermilion border of the lips, but is most often limited to the angles of the mouth. A wrinkled, adherent, sodden pellicle is formed beneath which is a reddened surface. There is no inflammatory areola, lymphangitis, or glandular enlargement. The duration is ordinarily two or four weeks, but may be considerably longer, and recurrences are common. The affected parts may retain a smooth, whitish appearance for several weeks after healing has taken place.

Perléche occurs chiefly in infants and children, and only occasionally in adults. The disease is highly contagious, and may be spread in families or schools by direct contact or through the medium of towels, drinking cups, and the like. Bacteriologic studies have shown the presence of a variety of microörganisms, and indicate that the streptococcus probably has an etiologic relation to the disorder. In all of Lane's cases the streptococcus was the only organism present in all cultures.

Treatment.—The prophylactic measures to be adopted are suggested by the foregoing account.

According to Lane, prompt cure is effected by daily applications to the lesions of a 10 per cent solution of silver nitrate, diluted tincture of iodin, copper sulphate, or the alum pencil. Two per cent ammoniated mercury ointment may also be used in the final stage, but not in conjunction with preparations of iodin.

Fordyce's Disease (*Pseudocolloid of the Lips*).—This is a benign chronic condition in which numerous discrete, yellowish, miliumlike spots are found projecting slightly above or more often embedded in the mucous membrane of the inner surface of the lips, and on the cheeks in the interdental region. The spots may be crowded together and form small patches, and are more prominent when the mucous membrane is stretched. There are no subjective symptoms and the condition is usually detected by accident.

Sutton and also Margolies and Weidman are of the opinion that the spots probably arise from invaginated, aberrant sebaceous buds, which increase in size at puberty along with the general hair and sebaceous gland systems. The duration is indefinite and retrogressive changes seldom occur.

Treatment.—The condition is a harmless one and treatment is usually not required or advisable. The spots may be reduced by freezing with carbon dioxid snow, and by the galvanocautery.

Periadenitis Mucosa Necrotica Recurrens (*Chronic Aphthæ*).—This disorder was first described in 1910 by Loblowitz and by Sutton independently, and a number of additional cases have since been recorded by others. Sutton describes the condition as beginning with a small, painless nodule situated beneath the mucosa of the lip, cheek, or tongue, which gradually enlarges, becomes smooth, hard, and painful, and during its development is attended by slight fever and by swelling and tenderness of the regional lymph glands. At the end of three or four days sloughing occurs, without suppuration, and a mummified-looking plug is detached, leaving a deep, painful and sensitive crateriform ulcer. The lesion heals within from six to eight days, with the formation of a soft, grayish, irregular scar. The lesions are usually single, though two or three may be present at one time and affect different mucous surfaces. Sutton states that the mucosæ of the cheeks and lips are affected with about equal

frequency, and that the sides and under surface of the tongue are attacked more often than the dorsum. Fordyce has observed lesions of the mouth and vulva in the same individual.

Cause.—The cause of the disease is unknown. It has been observed in infancy and in early adult life, and often persists for years. Histopathologic studies by Sutton showed the presence of an intense inflammatory process in the periglandular tissues, with necrosis, and separation of the central portion. Loblowitz believes it to be angioneurotic in origin and due to irritation of the vasomotor center by psychic stimuli.

Treatment.—The course of the disease is influenced only slightly, if at all, by treatment. Sutton observed benefit from outdoor sleeping, light exercise, and plentiful amounts of nourishing, easily digested food, with cod-liver oil, iron, and arsenic internally. Frequent applications to the ulcer of a 10 or 15 per cent solution of argyrol assist in reducing the secondary infection which is usually present, and decreases the pain incident to eating.

Herpes Labialis.—Herpes labialis, commonly known as "fever blisters" or "cold sores," is one of the regional forms of herpes simplex. It is an acute inflammatory disorder, characterized by an eruption on the mucocutaneous or adjacent cutaneous surface of the lips, of grouped vesicles, closely set or confluent, on an inflammatory base. The first manifestations are tingling, burning, and a sensation of tension in the affected area, followed by the formation of one or several groups of papules, which rapidly develop into clusters of vesicles upon inflammatory bases. The vesicles are of pinhead to small pea-size, and may coalesce into flat blebs. They contain a clear serum that later becomes turbid or milky and only rarely purulent. The vesicles desiccate or rupture, and form yellowish or brown crusts which become detached in a few days, leaving red stains and occasionally slightly depressed scars. Swelling of the regional lymph glands is often observed. The mucosa of the oral cavity, pharynx, and larynx may be the site of lesions, which in these locations are often bilateral and recurrent, and attended by mild systemic symptoms. Intact vesicles are rarely seen on the mucous surfaces, as they rapidly become eroded and form painful, superficial ulcers. There is a distinct tendency for herpes simplex in any situation to be recurrent, often in the same or identical areas, over a period of years, and this is especially evident in herpes of the mouth in adults. The recurrent forms are often associated with sensations of intense burning, neuralgic pains, and some constitutional disturbance.

Herpes simplex in any location appears to be due to irritation or inflammation in the terminal filaments of the peripheral nerves or ganglionic centers, as the result of local irritation, and bacterial, toxic or other systemic agencies. Herpes labialis occurs in a number of acute infectious disorders with considerable frequency, as in malaria, lobar

pneumonia, and cerebrospinal meningitis, but only rarely in typhoid fever and influenza. Its appearance during the course of an acute gastro-intestinal disorder is not uncommon, and in some individuals exposure to cold winds, or slight trauma to the lip, as may occur during shaving, is regularly followed by the herpetic eruption.

Lipschuetz and others have succeeded in inoculating the rabbit cornea with herpes simplex, and believe that the disease is due to a filtrable virus. Inflammatory and degenerative changes in the ganglionic centers have been found in herpes facialis occurring with acute infectious diseases. The histopathology is that of an acute inflammatory process with formation of vesicles in the rete.

Treatment.—In recurrent cases arsenic and quinin have been advised. Ormsby advocates radiotherapy for both immediate relief and prevention. When the disorder is due to gastro-intestinal intoxication, the treatment is obviously that appropriate to the underlying cause. Frequent local applications of spirits of camphor, of lotio alba (zinc sulphid and potassium sulphuret, each 60 gr., in 2 ounces of limewater), or of camphor in compound tincture of benzoin, are of service and will sometimes abort the lesions. Compound tincture of benzoin is a good protective after the vesicles have ruptured.

STOMATITIS

Acute or Catarrhal Stomatitis

Acute or catarrhal stomatitis is a disorder occurring at any age, but chiefly during infancy, characterized by hyperemia and swelling of any part or all of the oral mucosa, and by an increased secretion of saliva. It is produced by the local irritant action of food and drink which is acid or highly seasoned, too hot or too cold, by difficult sucking, the use of "pacifiers," mouth breathing, dentition in infancy, uncleanly conditions of the mouth, by carious and sharp-edged teeth, ill-fitting dental appliances, abuse of tobacco, and the like. It also occurs in gastric and intestinal disorders, and during the course of typhoid fever, measles, scarlet fever, small-pox, erysipelas, and influenza, being due in part to the original cause of these diseases and in part to lack of care of the mouth. The long-continued use of certain drugs, such as mercury, arsenic, iodin, bismuth, and others, predisposes to the development of this and other forms of stomatitis.

The local symptoms of catarrhal stomatitis consist in mild cases of small or more extensive patches of hyperemia of the oral mucosa, covered with viscid saliva, with swelling, and a moderate degree of pain. When the hyperemia is intense and extensive, the mucous membrane of

the lips and cheeks is swollen and often studded with cystlike vesicles due to distention of the mucous glands, a thin exudate covers the surface, and small patches of herpetic vesicles appear and are rapidly converted into grayish erosions. The papillæ of the tongue are often found enlarged and hemorrhagic at the tips. The saliva is thick, stringy and increased in quantity, and the breath is fetid. Pain is often severe and is increased by nursing or mastication. The neighboring lymph-nodes may be enlarged and tender. Constitutional symptoms, such as slight fever, anorexia, and restlessness, are usually observed only in infants. The course of the disease is acute, as a rule, and rarely lasts longer than a week.

Treatment.—Removal of the cause when possible, cleansing of the mouth, and attention to digestive conditions are required. Frequent washing of the mouth with tepid barley water or other similar demulcent preparations, containing 5 gr. of sodium bicarbonate to the ounce, which dissolves the mucous secretion, both cleanses and soothes the irritated mucosa. Mouth washes of 2 or 3 per cent solution of boric acid, 2 per cent sodium borate, dilute alkaline antiseptic solution (N. F.), or a weak solution of potassium permanganate, used at intervals of one or two hours, are also beneficial. Relief is also obtained by sucking small fragments of ice. Spongy bleeding gums should be touched with a 10 per cent solution of glycerite of tannin, and in obstinate cases a weak solution of nitrate of silver (gr. 1 to oz. 1) may be applied to the general mucosa once daily.

In bottle-fed infants the bottle and nipple must be carefully sterilized and the milk formula adjusted to the digestive requirements. After every nursing the child's mouth should be cleansed with sterile water, after which the antiseptic solution is applied with a cotton-tipped applicator. Constipation must be relieved and, if the skin is hot and dry, 1 dram doses of liquor potassii citratis may be given every two or three hours to a child of one year. As a prophylactic measure in the infectious diseases and other febrile affections, careful cleansing of the mouth with a mild antiseptic solution should be a routine procedure in the nursing care.

Aphthous Stomatitis

Aphthous stomatitis (vesicular stomatitis, herpes of the mouth) is an acute inflammatory affection characterized by the presence of one or numerous pin-point to split-pea-sized, oval, round or linear, shallow, grayish and painful ulcers, which appear in one or several successive crops, and are situated on the tip, edges, and under surface of the tongue, inner surface of the lips and cheeks, hard palate, floor of the mouth, and in the labiogingival fold. The lesions have their inception in small, bright red, highly sensitive macules, which are slightly elevated and may

resemble vesicles, and which rapidly assume a yellowish white appearance due to the degeneration of the surface epithelium. When this is cast off the characteristic sharply cut aphthous ulcer is left. The ulcers are usually single, but two or more may coalesce, and often two ulcers are situated opposite each other on the gums and on the lip. They are extremely sensitive and interfere with the movements of the mouth, and the condition is often further aggravated by a catarrhal stomatitis. Salivation occurs and may be pronounced, the breath is fetid, the mouth is hot and painful, and the submaxillary lymph glands are often enlarged and tender. Anorexia, thirst, nausea, restlessness, and moderate febrile reaction are also present. The disease runs its course, as a rule, in from four to seven days, though it may be prolonged for an additional week or two by the appearance of aphthæ in successive crops. In some individuals there is a marked tendency to recurrence, and any trivial derangement of health is followed by an attack of aphthous stomatitis.

The disorder is most common in children, especially between the ages of six months and three years, and is prone to occur in feeble, poorly nourished children during dentition, and in those affected with chronic diseases, especially of the gastro-intestinal tract, malaria, and the exanthemata. Adults, however, are often affected, frequent subjects being women at the menstrual periods, after parturition, and during lactation.

A confluent form of aphthæ, probably differing in etiology from the ordinary variety, has been observed in children. It is either primary or secondary to one of the exanthemata, typhoid fever, diphtheria, pneumonia, pertussis, or gastro-intestinal disorders, and is a serious affection. The ulcers are resistant to treatment, there is fever and rapid emaciation, and a toxic erythema may appear and constitute a grave symptom. After lasting two or three weeks the disease may terminate in bronchopneumonia or meningitis. A fulminant variety has also been described, ending fatally in one or two days after the development of the aphthæ, with fatty degeneration of the liver as the prominent postmortem finding. In these forms various round and rod-shaped organisms and Vincent's spirilla are found on bacteriologic examination.

Etiology.—The etiology of aphthous stomatitis is undetermined. Bacteriologic investigations have shown the presence of various organisms, which, however, are also normal inhabitants of the mouth. Gastro-intestinal disorders are generally considered as causative, but the lesions are probably due to an infection. Its contagiousness has not been established, though it often occurs in institutions for children, and in several members of the same household.

Treatment.—This usually requires attention to the gastro-intestinal tract, with such correction of the diet as is necessary, and relief of constipation or diarrhea. In artificially fed infants sterilization of bottles and nipples must be enforced, and the food mixture properly modified

to meet the demands of the individual case. Older children should be given a simple, nourishing, liquid diet, which includes broths and rice. An antacid laxative, such as rhubarb and magnesia or soda, or calomel followed by magnesia, may be given when constipation is present and, if there be diarrhea, castor oil or high bowel flushing may be indicated.

The mouth should be frequently cleansed with mild antiseptic washes and demulcent alkaline mixtures as described under Catarrhal Stomatitis. Potassium chlorate is of doubtful value. Cleansing of the mouth in infants should be done with extreme care to avoid injury to the mucous membrane. The ulcers may be touched with the nitrate of silver stick, or with a 1:150 solution of potassium permanganate. Starr prefers the thorough application of a minute quantity of trichloracetic acid to the floor of each ulcer by means of a pointed wooden applicator. Just enough distilled water is added to the acid crystals to insure deliquescence, and, after it has acted upon the ulcer for about one minute, sodium bicarbonate may be applied to neutralize the acid. One application usually suffices to relieve pain and induce healing.

Bednar's Aphthæ

Bednar's aphthæ consist of two, rounded, shallow, gray or yellowish ulcers, symmetrically situated over the hamular processes of the palate bones, or they are Y-shaped and linear when situated over the palatine suture and the line of junction of the hard and soft palate. They occur only in the newly born, appearing from the second day to the sixth week, and are due to traumatism by the nurse's finger during cleansing of the mouth. The friction of an improperly shaped rubber nipple during the act of sucking, thumb sucking, and prolonged sucking at an empty nipple may result in the development of an ulcer on the anterior part of the hard palate.

Treatment.—The ulcers usually heal readily after removal of the cause and under gentle washing with a mild antiseptic solution. If the ulcers are indolent they should be carefully touched with a 10 per cent solution of silver nitrate. In bottle-fed infants nourishment may be given by spoon or with a medicine dropper.

Hyphomycetic Stomatitis

Hyphomycetic stomatitis (parasitic or mycotic stomatitis, thrush) is characterized by the formation of adherent, white, curdlike flakes and patches upon the mucous membrane, due to infection with a fungus, the Oïdium albicans. The oïdium is a pleomorphic organism, occurring as small yeastlike cells and as filaments, both of which are usually found together in the mouth. This pleomorphism has been the cause of the

uncertainty which has existed for years as to the identity of the causative organism of thrush. Recent researches by Fineman show that the oïdium when artificially cultivated tends to assume the mycelial or filamentous form in liquid mediums and under special chemical and physical conditions, while the yeastlike form occurs in solid mediums and under other special conditions, and it is suggested that the pleomorphism is an attempt at adaptation.

Thrush usually begins with a dusky hyperemia, heat, dryness and tenderness of the mucosa, soon followed by the formation of small circular, white spots on the tip and edges of the tongue and inner surface of the lips and cheeks. The spots rapidly enlarge and become fused into irregular patches resembling flakes of curdled milk, which are closely adherent, and when forcibly removed leave a number of bleeding points. The patches may be scattered and few in number, or the deposit may cover the tongue, extend along the gingivobuccal folds, and cover the entire inner surface of the mouth. The pharynx, esophagus, nose and larynx may be invaded and, in rare instances, the stomach is involved. In the feeble and cachectic it also occurs about the anus and genitalia, and extensive invasion of the skin has been observed. The patches consist of the fungus, epithelial cells, and leukocytes. From one to two weeks after their first appearance, the patches loosen and expose superficial abrasions, and at times large masses are exfoliated, leaving intractable ulcers. The mouth is usually dry and extremely sensitive, and the taking of food is a painful task. There may be slight fever, and sometimes vomiting and diarrhea.

Thrush is most common in the first two or three months of infancy, but may occur during any period of childhood, and, in adult life, in individuals of impaired vitality. In infancy it is most frequent in poorly nourished, neglected, and marasmic subjects, in whom simple colds and slight gastro-intestinal derangements favor the development of the infection. Injury of the mucosa by too vigorous or unskillful cleaning of the mouths of infants, and by difficult sucking, provides a locus for the infection, which also may be transmitted in nurseries by unclean feeding bottles and nipples. In older children and in adults, usually the aged, it appears in pneumonia and the exanthemata, and in the final stages of chronic wasting diseases.

Unless neglected, thrush, as ordinarily encountered, readily yields to treatment, but in conditions attended by marasmus or cachexia it is apt to be a serious complication.

Treatment.—As a preventive measure in infants, the mouth should be gently cleansed once daily with absorbent cotton moistened with a saturated solution of boric acid; and bottles, nipples, and spoons used in feeding should be sterilized by boiling. Abrasions of the mucosa should receive prompt attention. When patches are present, frequent

cleansing of the mouth with boric solution or 2 per cent sodium bicarbonate solution is required, using separate pledgets of cotton for the tongue and the different parts of the mouth. Starr recommends the application of vaselin to the patches to facilitate their removal, followed by brushing with boric acid solution to prevent redevelopment. Potassium permanganate solution (1:150), copper sulphate (2 gr. to the ounce), and 1 to 2 per cent silver nitrate solution are useful as local applications to obstinate patches. Constitutional treatment is based on the indications presented by the underlying conditions, and usually includes tonic and supporting measures, with attention to proper hygiene.

Ulcerative Stomatitis

Ulcerative stomatitis (putrid sore mouth, phlegmonous stomatitis) is a term applied to ulcerative conditions in general, arising as the result of local irritation from improper dental appliances and neglect of oral hygiene; certain of the infectious diseases; scurvy; poisoning with mercury, iodin, lead, and phosphorus; leukemia, and other debilitating conditions. It occurs in children after dentition and in adults. In addition to the common pyogenic organisms, the fusiform bacillus of Vincent, associated with spirochetes, is nearly always present. The same organisms are found in a variety of disorders with ulceration, such as scurvy, ulcerating carcinoma of the mouth, noma, and others; and, while they are probably important agents in the production of the condition, a specific etiologic relation is not proved. In the writer's opinion it is not unlikely that the conception of Vincent's disease or ulceromembranous stomatitis and angina will eventually be broadened to include much of what is now termed ulcerative stomatitis.

The process begins as an acute gingivitis, attended by pain and heat in the mouth. The margin of the gum rapidly softens into ulcers with red, swollen margins and a grayish or brown necrotic floor. In its further development the ulcerative process may extend along the labial and palatal surfaces of both the upper and lower gums, the edges of the tongue, and along the buccal mucosa contiguous to either the upper or lower, or both, gum margins. With increase in depth and extent of the gingival ulceration, the teeth become loose and may drop out, and destruction of the periosteum and extensive necrosis of the maxillary bones may occur. This destructive feature is observed most often in children, particularly between the ages of five and twelve years, and is attributed by Brown to "the fact that the jaws are, at this particular time, so filled with developing teeth that the actual bone resistance and blood circulation are reduced, and also because at this period the diseases incident to childhood, both local and general, predispose to infections of this character." Salivation is profuse, the breath is extremely fetid,

and the mouth is hot and painful. The face may swell from inflammatory edema, and the submaxillary and cervical lymph glands enlarge but rarely suppurate. Nourishment is taken with difficulty, there is slight fever, anorexia, nausea, and progressing exhaustion. In debilitated children the outcome may be fatal.

The duration is about ten days in the ordinary case, but severe or complicated cases may require a month or more for recovery.

Treatment.—Isolation of the patient in well-ventilated quarters, with plenty of sunlight, is of first importance, along with removal of the cause if this be possible. The diet should be liquid and nutritious, and water must be given freely. Potassium chlorate has an almost specific influence, although its toxic properties must always be kept in mind. Starr advises 1 gr. doses every two hours for a child of three years, given in water or with a bitter tonic, such as elixir of calisaya. Adults may take from 10 to 20 gr. three or four times a day, and it is also effective in a mouth wash containing from 10 to 20 gr. to the ounce. It should not be used over a prolonged period.

The mouth must be kept clean by the liberal use of washes, such as the alkaline antiseptic solution, and hydrogen peroxid diluted with from 2 to 10 parts of water. Frequent use should be made of the solution of potassium chlorate, both as a mouth wash and for local application. Continuance of ulceration, in spite of internal and local treatment, is an indication to search for and remove a local cause, such as carious or sharp teeth, roughened borders of the alveolar process, dental crowns and bridges, and necrosed bone. Sound teeth if loosened by the ulceration usually regain their firm position after recovery, but in some instances it may be necessary to extract teeth about which ulceration persists before healing can occur. Usually, however, the ulcers are responsive to applications of tincture of iodin, solutions of silver nitrate or the solid stick, and especially to potassium permanganate. When the ulcerative process has ceased, tonics of iron, quinin, and nux vomica will be found useful in most cases.

A chronic form of ulcerative stomatitis has been described, which presents the same, though milder, oral symptoms, runs a protracted course with frequent relapses, is resistant to treatment, and does not involve the deeper tissues.

Mercurial Stomatitis

Mercurial stomatitis develops when the individual's limit of tolerance for the metal has been exceeded. Some persons have an idiosyncrasy to mercury and one or several small doses suffice to produce salivation. Chronic nephritis and hepatic cirrhosis predispose to its development. In a properly regulated course of mercurial treatment, salivation should

never occur. Its onset is preceded by slight tenderness of the gums with a tendency to bleeding, an increase in the amount of saliva, a sensation of soreness in the teeth when they are forcibly snapped together, some fetor of the breath, and gastro-intestinal symptoms. If the mercurial is not at once discontinued the mucosa becomes red and swollen, there is profuse salivation, the tongue is tumified and covered with a dirty-grayish, slimy coat, and sloughing ulcers may develop upon its margins and on the buccal mucosa where the teeth impinge upon them. The condition present is that of an ulcerative stomatitis, with a horrible fetor, and at times an extensive ulceration of the tonsillar and faucial regions. The patient is much reduced and death may result from septic infection or an accompanying enteritis.

Treatment.—The administration of mercury should be discontinued upon the first indication of ptyalism and, if it has been introduced intramuscularly by injection as an insoluble salt, the deposit should be removed surgically. The mouth should frequently be cleansed with peroxid of hydrogen (2 or 3 per cent) and with a tepid solution of potassium chlorate. In mild forms tincture of myrrh and cinchona, locally, will be found useful. In severe cases it has been recommended to lay strips of iodoform gauze in the mouth, or to dissolve a 1-gr. pill of iodoform in the mouth three times daily. Potassium chlorate should also be given internally in 2 or 3-gr. doses every two hours for an adult, and in severe cases it may be given to the extent of 60 gr. daily. The food should be liquid and nutritious; iced drinks or foods in particular must be avoided as gangrene may occur from their use.

Bismuth Stomatitis

Bismuth salts may cause characteristic symptoms of poisoning in some individuals when used in the treatment of sinuses, in radiographic work, as intramuscular injections for the treatment of syphilis, or as dressings for extensively denuded areas such as burns. Animal experimentation indicates that the paths of elimination of the metal determine the occurrence of stomatitis, nephritis, and enteritis as characteristic symptoms of intoxication. Fatal cases have been reported with acute symptoms—cyanosis, collapse, diarrhea, and methemoglobinemia—like those described in nitrite poisoning. Bismuth subnitrate under certain conditions liberates nitrites and these may be responsible for the acute intoxication observed in certain cases of intestinal disease. In the chronic forms, and in those in which bismuth has been used on denuded areas, bismuth itself is the toxic agent.

Warfield describes three stages of chronic bismuth intoxication: a violet-black line; an acute stomatitis followed by pigmentation of the buccal and gingival mucosa; and a severe form with stomatitis of longer

duration, ulcerations, and secondary infections, attended by fever, hiccough, vomiting, diarrhea, and albuminuria. The characteristic feature is the violet-black or dark plum-colored line on the gums, with tattoo-like patches on the buccal mucosa, and bands or diffused areas of pigmentation beneath or on the sides of the tongue. The larger patches on the cheeks and tongue may develop shallow ulcerations and are often covered with a white diphtheritic membrane. Gangrene may occur in severe cases, and the soft palate and tonsils may be ulcerated. The lesions usually develop rapidly with edema of the affected area, and are often preceded by hyperemia of the oral mucosa and mild salivation. When once established the discoloration remains for a long time after all other symptoms have disappeared. Severe forms of bismuth stomatitis resemble those due to mercury; there is profuse salivation, fetor of the breath, swelling of the gums, ulceration and gangrene, loosening of the teeth, albuminuria with casts, general exhaustion, and in addition the urine may be blackish and frequently contains bismuth.

Treatment.—Warfield recommends that care should be taken that the bismuth paste in sinuses is gradually extruded, and, if it remains deep in the sinus, its early removal is advised. Its use on large raw surfaces should be avoided, and bismuth used in X-ray work in the intestines should be withheld in inflammatory cases or in patients who are much run down in health. Frequent flushing of the mouth with antiseptic and demulcent washes is indicated, with applications of argyrol or other similar preparations to the ulcers, and equal parts of tincture of myrrh, nutgall and krameria to the gums. Systemic treatment is similar to that discussed under Mercurial Stomatitis, with particular attention to the kidneys and intestine.

Gangrenous Stomatitis

Gangrenous stomatitis (noma, cancrum oris) is a fulminating gangrene of the cheek, occurring in the course of or as a sequel to the acute exanthemata, especially measles, diphtheria, typhoid fever, pertussis, dysentery, scurvy, and ulcerative stomatitis. More than one-half of the recorded cases have been preceded by measles, and it is usually associated with or follows an ulcerative stomatitis. It is rare in infants and adults, and usually affects weak and ill-nourished children between the ages of ten and twelve years. It is probably contagious. The cause of noma is unknown, though it has been variously ascribed to the bacillus and spirillum of Vincent, the Klebs-Loeffler bacillus (Walsh), an anaërobic bacillus found also in hospital gangrene, and to several other bacteria.[2]

The first symptoms of noma are salivation, fetid breath, and the presence of a small, painful nodule in the tissues of the cheek, surmounted

[2] It occasionally assumes an epidemic form in institutions.—Editor.

by a dark-colored bulla on the buccal mucosa between the commissure of the mouth and the opening of Steno's duct. The base of the bulla rapidly disintegrates into a blackish, soft, necrotic mass, and the gangrenous process extends in depth and peripherally. The skin over the induration is at first swollen, tense and waxlike; soon a purplish spot appears, gradually becomes gangrenous, and perforation of the cheek occurs with subsequent necrosis extending in all directions. The entire cheek, the greater part of the nose and lips, the gums, alveolar processes, tongue and palate may be involved by the gangrenous process. Severe pain is rare and extensive hemorrhage is prevented by the early formation of thrombi.

The constitutional symptoms are mild in the beginning, and the pulse and temperature are almost normal; but, as the disease progresses, high fever of a hectic character develops, with delirium and frequently a septic diarrhea, and death results from exhaustion or bronchopneumonia. The mortality is about 70 per cent; many patients die within three or four days, and some survive for one or two weeks. Recovery may occur before the cheek is perforated, but ordinarily great disfigurement remains.

Welch and Schamberg describe a less serious form of gangrenous stomatitis, beginning about the gums and alveolar process, in which the necrosis is limited to the mucous membrane and bony tissues of the mouth. After the loss of some of the teeth and a portion of necrosed alveolus, the process may cease and recovery take place.

Treatment.—The development of stomatitis in the exanthemata, particularly measles, calls for frequent and thorough cleansing of the mouth with antiseptic solutions, such as potassium permanganate, and painting of any denuded or ulcerated areas with tincture of iodin or argyrol. If noma develops and is detected early, the necrotic area in the mucosa must be promptly curetted away under a general anesthetic and the base thoroughly cauterized with fuming nitric acid, the acid solution of nitrate of mercury, or the Paquelin cautery. If the skin of the cheek shows evidence of gangrene or impending gangrene, the involved area must be at once widely excised and the edges thoroughly cauterized with the Paquelin cautery. The wound is to be dressed antiseptically, using iodoform and potassium permanganate or hypochlorite solutions, which also serve as deodorants, and the mouth should be cleansed by frequent syringing with the same solutions and with hydrogen peroxid.

It is of prime importance to maintain the patient's strength by the liberal use of nourishing liquid food, quinin, strychnia, iron and alcoholic stimulants. Diphtheria antitoxin should be given in those cases in which the diphtheria bacillus is present.

Plastic surgery for the correction of deformities should not be done for a considerable period of time after recovery, as an early operation may induce recurrence.

Gonorrheal Stomatitis

Gonorrheal stomatitis is an infection of the mucous membrane of the mouth by the gonococcus of Neisser, and usually occurs in infants from five to twelve days after birth, the infection in most instances being derived from the mother during parturition.

Yellowish white patches are present on the pillars of the fauces, the posterior part of the upper jaw, the gums anteriorly, and sometimes on the frenum of the tongue and lips. The patches tend to be symmetrical and remain stationary, and are not accompanied by diffuse inflammation of the mucosa, but are surrounded by a narrow hyperemic zone. Systemic symptoms are absent and recovery takes place in from five days to three or four weeks. In adults, however, marked systemic disturbance, pain and burning are present, the entire oral mucosa is acutely inflamed, an exudate is formed, there is a profuse discharge, and shallow ulcers may develop.

Treatment.—Infection of the conjunctival sac must be prevented by instillation of silver salts and observance of absolute cleanliness. Protargol, argyrol or silver nitrate solutions (1 to 2 per cent), or a 1:7,000 solution of bichlorid of mercury, applied twice daily, are curative remedies.

Unclassified Forms of Stomatitis

Recorded in the literature are forms of stomatitis which remain unclassified. They differ from stomatitis as usually encountered in several important particulars, and are usually a prominent feature in a complex of symptoms. Their etiology is obscure, though in most instances the entire process, of which stomatitis is an important part, appears to be of septic origin.

Such is the syndrome described by Widowitz, characterized by severe membranous stomatitis, toxic cutaneous eruption, and a tendency to the development of thoracic empyema. Following a prodromal period of from four to seven days with symptoms of marked exhaustion, a rapidly extending ulceromembranous inflammation of the mucous membranes of the mouth, nose, pharynx, and at times the conjunctiva develops. Ten days after the onset a toxic cutaneous eruption appears expressed as an erythema multiforme, a scarlatiniform exanthem or as a folliculitis. There is great prostration, bronchopneumonia develops, and in two weeks from the onset a pleural empyema is demonstrable. He observed 4 patients with this affection, children from six to nine years old, of whom 2 died. The stomatitis resisted all forms of treatment. In the mouth only the ordinary bacteria were present, and streptococci were found in the empyema.

Kundratitz has recorded an instance of severe ulceromembranous

stomatitis resistant to treatment and of unknown etiology, associated with diarrhea, collapse, hyperpyrexia, and a fleeting cutaneous erythema, which he believes belongs to the group described above.

Stevens and Johnson have described as a new clinical entity a syndrome comprising a bullous stomatitis, purulent conjunctivitis, and a maculopapular cutaneous eruption with later pigmentation, attended by severe systemic reaction. The duration is three or four weeks and leukopenia is a feature. The writer has seen an almost identical condition in a patient of VanValzah's, with bullous stomatitis, purulent conjunctivitis and a sparse eruption of petechial character.

Treatment.—In all such anomalous conditions it is advisable to enforce isolation, preserve the strength and resistance from the outset by an abundance of nourishing food, preferably in liquid or semiliquid form, and to secure proper elimination. Many of these as yet obscure conditions in which stomatitis is a prominent feature are of grave import and require stimulating treatment early. The mouth should be cleansed every hour or two with a weak solution of hydrogen peroxid followed by an alkaline mixture or a demulcent, such as oatmeal or barley water. Denuded areas should be touched with argyrol or a weak solution of silver nitrate.

ERUPTIONS DUE TO DRUGS

Numerous drugs are capable of producing eruptions which develop as the result of an individual hypersensitiveness or allergy, or of defective renal elimination. In most instances the eruption is cutaneous, in a small number both the skin and oral mucous membranes are affected, and only rarely is the mucous membrane alone involved.

Antipyrin causes a variety of reactions in the mucosa with a pronounced tendency to the formation of erosive lesions recurrent at the same site, or of diffuse bullous or pemphigoid lesions. The lips, buccal mucosa, palate and tongue are often swollen and painful and extensive epithelial exfoliation may occur. *Salipyrin* has produced swelling of the lips, gums and palate with an eruption of vesicles in the mouth. Stomatitis occurs in some of the cases of exfoliative dermatitis due to *arsphenamine*. *Chloralamid* has caused congestion of the oral mucosa. *Potassium iodid* may produce vesicular, bullous, erosive and condylomatous lesions on the tongue, palate and fauces. *Phenolphthalein,* which is contained in many of the proprietary laxative compounds, causes erosive lesions of the lips, buccal mucosa and tongue. Stomatitis with superficial ulcerative lesions has followed the use of *luminal* (phenobarbital) and *trional; quinin* has produced edema of the lips, and *salol* an eczema of the lips. *Veronal* has caused painful swelling of the entire oral mucosa, with a vesicular eruption and erosions, attended by fever.

Treatment.—Discontinuance of the drug and the use of laxatives and diuretics is usually followed by rapid disappearance of the oral symptoms. Cleansing mouth washes and local applications of silver salts promote healing.

ORAL MANIFESTATIONS OF CUTANEOUS DISEASES

The occurrence of macules and papules, and of vesicular and exudative processes in the mucous membranes, resulting in erosions, plaques and ulcerations, is observed as part of the symptomatology of a number of cutaneous and other diseases. Among the disorders usually classified as typically cutaneous, but in which the oral mucosa may also be involved, are lichen planus, erythema multiforme, dermatitis herpetiformis, the three varieties of pemphigus, erythematous lupus, lupus vulgaris, herpes and impetigo herpetiformis, mostly dermatoses of constitutional origin. Involvement of the mucous membranes is of frequent occurrence in several of these conditions and may, in fact, precede the cutaneous symptoms or, in rare instances, be the only manifestation of the disease.

Lichen Planus

Lichen planus is an inflammatory dermatosis characterized by small, angular, flattened, red or violaceous, papules, which tend to coalesce into scaly patches. It usually pursues a chronic course with a limited distribution of its lesions, but may be acute, and at times develops as an extensive or even generalized eruption. The duration is variable, lasting for months or rarely years, and relapses are not unusual.

Lichen planus affects the mouth in about one-third to one-half of the cases, the buccal mucosa opposite the interdental space about the molar teeth being the site of predilection, with the tongue and lips as the next most frequent sites. The essential lesion is a papule, appearing as a convex, conical or flattened, firm, whitish gray dot of pinhead size or smaller. The papules are either discrete and scattered, or arranged in groups or lines, the latter often forming a characteristic meshwork with nodes at the points of intersection. Circinate lesions may be formed by central involution and peripheral extension of large papules or, more often, by the appearance of new papules at the margin of an older group, with involution of the latter, leaving a depressed, smooth, non-striated, bluish red center with a delicate polycyclic border composed of tiny papules.

On the dorsum of the tongue the lesions occur as circular, or more often oval, grayish, lentil-sized patches, discrete or fused, varying from few to a dozen or more in number, and often symmetrically arranged, with

an appearance as though painted on velvet. On the borders and under surface of the tongue they appear as dull gray, smooth, irregular bands or stripes, or as solitary papules. On the labial mucosa the papules coalesce into irregular plaques, and on the vermilion border dry, slightly desquamating patches are formed with an elevated, festooned border nearest the cutaneous margin. On the mucosa of the hard palate, soft palate, and gums the lesions occur more often as distinct papules than in patches or networks.

When of long standing the lesions in any situation become less distinct, are smooth, white, and resemble silver nitrate stains. Erosion, ulceration and scar formation do not occur. Pain is unusual, but the lesions are hypersensitive to hot or spicy foods. Lichen planus of the mucosa is an indolent affection and often responds less readily to treatment than do the cutaneous lesions.

Etiology and Pathology.—The cause of lichen planus is unknown. The prevailing view is that toxemia and nervous disturbances are essential factors. Others, including the writer, believe that lichen planus is a microbic disease. The histopathology is characteristic and shows a circumscribed infiltration of connective tissue cells and lymphocytes in the papillary layer of the corium, with edema; marked hypertrophy of the rete mucosum, granular layer, and stratum corneum, with some colloid degeneration.

Treatment.—This consists in attention to the gastro-intestinal tract, good hygiene, and the use of cod-liver oil and of tonics when indicated to improve the general health. Arsenic is a valuable remedy in the subacute and chronic cases, though it often fails, and may be given internally as liquor potassii arsenitis or Fowler's solution in ascending doses. Mercury is considered by many, including the writer, as superior to arsenic in this disease, and is given by mouth as hydrarg. protoiodid (gr. ⅛ to ¼ in pill three times a day) or hydrarg. biniodid (gr. 1/24 to 1/16 in cinnamon water three times a day). More rapid and lasting results are obtained from deep intramuscular injections of hydrarg. bichlorid in doses of from ⅛ to ¼ gr. given every second day for about twelve doses. Intramuscular injections of enesol (mercury salicylarsenate) have also been recommended. Arsphenamin has not proved satisfactory in this disease. When using arsenic and mercury the possible toxic effects of these remedies must be borne in mind.

Carious teeth should receive dental attention, sharp-edged teeth must be ground smooth, and dental plates fitted properly or removed. When the mouth lesions are troublesome or extensive a mouth wash such as liquor alkalinus antisepticus (N. F.) may be used, with local applications of argyrol or of a solution of potassium permanganate. Main reliance, however, is to be placed on constitutional medication with mercury or arsenic.

Lupus Erythematosus

Lupus erythematosus is a chronic, sometimes acute, inflammatory disease of the skin, characterized by erythematous, scaling patches, which tend to persist, gradually undergo atrophic changes, and are replaced by superficial scars. Clinically, two main types are recognized, the circumscribed or discoid type, chronic in its course, and the disseminated or diffuse type which is more or less acute. The chronic discoid type is by far the more common.

Involvement of the mucous membranes of the lips and mouth is not unusual, and occurs either by direct extension from the cutaneous surface or independently. In some instances lupus erythematosus may be confined to the mucous membranes, either entirely, which is rare, or for a considerable time preceding its appearance on the skin or scalp. The course of the lesions on the mucosæ is, in general, that of the chronic discoid cutaneous type, and consists of an active inflammatory stage, followed by an inactive atrophic stage, with exacerbations at irregular intervals.

Lupus erythematosus on the oral mucosa usually begins as one or more hyperemic, bluish red, edematous, slightly elevated patches, with indefinite outlines and, at times, a slightly eroded surface. Within a few days the margins become slightly elevated and more distinct in outline, and delicate vascular striations are seen converging toward the center, which is now depressed, eroded, and often covered with an adherent yellowish pellicle. After a variable length of time the central erosion increases in depth and is either converted into a thin, flat scar, or is covered with epithelium, with the formation of closely set, bluish white puncta or striations converging centrally. Coincident with the appearance of these striations the lesion loses its inflammatory character and enters on the stage of atrophy and quiescence.

It is not unusual, however, for the lesion to enlarge again by peripheral extension and to show recurrent central erosion at intervals.

Lupus erythematosus often attacks the lips, especially the mucous surface of the lower lip, and in this location presents distinctive features. One or more patches may develop and by confluence involve the entire lip, which becomes violaceous, swollen, and is often everted. In acute stages the lip is covered with large, thin epithelial lamellæ and with blood crusts, and resembles a peeling coat of collodion. Beneath the scales irregular, red, eroded areas are seen on the violaceous labial mucosa, which is stippled with white dots. On the lips the lesions cause much discomfort and bleed on the slightest movement, a condition rarely observed in lesions of the oral mucosa, which often remain unnoticed by the patient.

On the tongue the disease is manifested in flat, smooth, grayish spots,

about 3 or 4 mm. in diameter, in larger, irregular, smooth, deep red patches denuded of papillæ, or in smooth leukoplakic patches with a reddish halo. Lesions of the tongue are not uncommon.

The mouth lesions found in association with the acute disseminated form of lupus erythematosus often present a close resemblance to the lesions of tuberculosis. They are deep or shallow ulcerations, irregular in shape, with soft, partly overhanging, fringed edges, and are covered with a necrotic, grayish yellow film or exudate.

Etiology.—The cause of lupus erythematosus is unknown. It is generally held at present that the acute disseminate variety is probably tuberculous in origin, and Stokes has called attention to its frequent association with mesenteric tuberculosis. The circumscribed or discoid variety, however, is probably of toxic origin, diverse in nature and source. Focal infections of the teeth or tonsils in some instances appear to be an etiologic factor.

Pathology.—The nature of the histopathologic changes is still in dispute. The disease process is found mainly in the upper half of the corium as a dense infiltration of small round cells of embryonic type, chiefly along the vessels, with hypertrophy of the sebaceous glands, followed by degeneration and atrophy, and degenerative changes in the collagen. In lesions of the mucous membranes the epidermis is thickened, the mucosa cornified, and the corium is infiltrated with lymphocytes, connective tissue cells, and plasma cells.

Treatment.—There is no drug or chemical known at present that exerts a specific influence on the disease. Quinin in 10 or 15-gr. doses, arsenic in torpid lesions, ichthyol in the active stages, the salicylates, and numerous other remedies have been advocated and are occasionally beneficial. Constitutional measures designed to improve the general health, such as a hygienic mode of living, adoption of a proper dietary, removal of sources of focal infection, and the administration of tonic medication adapted to the individual's needs, are of benefit though not directly curative. Tuberculin cannot be recommended for diagnosis or treatment, and harmful effects have followed its use in this disease. Autogenous streptococcus vaccine obtained from the enucleated tonsils, autogenous colon vaccine, and mixed streptococcus vaccine have been used with benefit in some cases.

Hot foods and beverages, highly spiced foods, hard and coarse foods, and the use of tobacco and medicated dentrifices are liable to aggravate the lesions through their local irritant action, and should be forbidden. For the same reason, sharp or roughened teeth must be ground smooth, and the proper fit of dental plates assured.

The local treatment is unsatisfactory as a rule. Energetic measures must be avoided as they encourage extension. In most instances the lesions cause no inconvenience, and a non-irritant mouth wash, such as the alkaline

antiseptic solution (N. F.), and local applications several times a day of a 5 per cent solution of argyrol meet the indications.

Trichloracetic acid applied directly to the lesions in 50 per cent solution is a local remedy of some value. Wise applies it once in two weeks, and repeats the application when the crusts have separated. It is advisable to neutralize the acid soon after its application by means of a saturated solution of sodium bicarbonate. Electrocoagulation is given preference by some over other methods. Small torpid patches have been successfully removed by the use of carbon dioxid snow, using moderate pressure for ten seconds, with the surface thoroughly dried. Good results have also been obtained with radium, but with this agent, as with practically all local methods, great care and good judgment are necessary to avoid injurious effects. The ultraviolet rays produced by the Kromayer water-cooled lamp are advocated by some, but the writer has failed to secure good results with this method.

Erythema Multiforme

This is an acute inflammatory disease characterized by an eruption of bluish red macules and papules, and of vesicles and bullæ, usually symmetrically distributed on the face, neck and extensor surfaces of the extremities. One type of lesion predominates as a rule, and when this is vesicular or bullous the eruption frequently also involves the mouth, tongue and lips. Lesions may develop in the mouth before the cutaneous eruption appears or, in rare instances, may remain limited to the mucosa.

In the variety designated as herpes iris the lesions on the mucosa occur as small concentric vesicular rings; this form of the disease tends to be recurrent. As usually observed the mucous membrane lesions in erythema multiforme are vesicular and bullous, developing rapidly on an hyperemic base, with sensations of burning and tingling, and rupture early, leaving painful, deep red, coin-sized erosions, covered with a fibrinous exudate. The tongue may be swollen, and when the mucosa is extensively involved there are symptoms of toxemia of varying degree and fever. Although the disease most often pursues a mild course, with few systemic symptoms, it may in some cases be a formidable affection of extreme gravity. The prognosis is practically always favorable, the attack ending in from ten days to four weeks, but the disease is apt to recur over a period of years, usually in the spring and autumn months. In those cases in which the eruption is part of a systemic disorder, the prognosis depends upon the nature and gravity of the underlying condition (see article on the Visceral Manifestations of Erythema, Vol. IV, p. 43).

Etiology.—The cause of erythema multiforme has not been established, but low-grade infections are probably the most frequent etiologic factor. The frequent association with mild arthritic symptoms would

also point to such origin. It may follow the use of certain drugs, such as potassium iodid, mercury, and coal-tar derivatives, of stale articles of food, and the use of antitoxic sera, and it occurs in connection with vaccination, microbic infection, and visceral diseases. The disease is an inflammatory process, the character of the lesions being determined by variations in the amount of exudation.

Treatment.—The disease is self-limited and internal treatment is chiefly symptomatic and in most instances is designed to correct gastro-intestinal disturbances and improve elimination. Lactic acid bacilli may be of value, but intestinal antiseptics as ordinarily recommended are useless. In all cases and especially in those in which "rheumatic" pains are present in the muscles and joints, the lymphatic structures of the throat should be investigated as possible sources of infection. The writer has seen several instances in which erythema multiforme was definitely due to tonsillar infection. The existence of apical abscesses and of sinus infection should also receive consideration. Alkalis and salicylates are of distinct value in many cases. Sodium citrate, sodium bicarbonate, and sodium salicylate may be given freely with copious amounts of fluids. When the mouth lesions are extensive it may be necessary to resort to proctoclysis, and solutions of sodium bicarbonate containing sodium salicylate may be given in this way. In periodically recurrent cases a course of intestinal antiseptics and occasional purgation previous to the usual time of the outbreak will, Stelwagon believes, sometimes ward off the attack.

The mouth should be kept clean by the frequent use of a solution of permanganate of potash or other alkaline antiseptic solution, and argyrol in 10 per cent solution may be applied several times a day. As a useful application to painful erosions Ormsby recommends 15 drops of iodized phenol in one-half glass of water.

Pemphigus

Pemphigus is an acute or chronic disease of the skin, characterized by the rapid development of bullæ, often on apparently normal skin, accompanied by constitutional symptoms of varying degree. It is a rare disorder and occurs in four clinical varieties: pemphigus acutus, vulgaris, foliaceus, and vegetans. Pemphigus acutus occurs in connection with septic wounds and vaccination, runs a rapid course with severe systemic symptoms, and is often fatal. The bullous eruption is usually widespread, often hemorrhagic, and tends to involve the mucous membranes. It is an expression of a general sepsis, and its inclusion in the group of true pemphigus is open to question.

In other varieties of pemphigus the disease may begin with one or more bullæ in the mouth, pharynx, on the lips or conjunctiva, and may re-

main limited to these localities for weeks, months, or rarely for years before lesions appear on the skin. Without premonitory symptoms superficial bullæ suddenly appear anywhere on the oral mucosa, rupture almost at once, and leave a painful, readily bleeding, superficial erosion with shreds of epithelium at the margins, and a peripheral zone of inflammation. The erosions become macerated and form diphtheroid patches, which may present polycyclic contours by fusion of adjoining lesions. The tongue is sometimes enveloped in a necrotic membranous cast which can be stripped off in one piece, leaving a raw, bleeding surface. Instead of rupturing early some of the bullæ may persist for several days and be absorbed unruptured. There may be few lesions or the process may be extensive and involve the entire oral mucosa. Regeneration of the mucosa is rapid and complete, though sometimes sluggish. Pain is often severe and prevents taking of food, with consequent malnutrition; the breath is foul, there is some salivation, and the submaxillary glands are swollen. Periods of partial or complete remission may occur and delay the ultimate fatal outcome for months, or years, or the disease may be rapidly fatal. At times, though rarely, all the lesions of pemphigus disappear shortly before death occurs. Pemphigus which begins with lesions in the mouth is apt to run a short and severe course, though exceptions to this are frequent.

Etiology.—The cause of pemphigus is unknown. It is not contagious and heredity is not a factor, though the Jewish race appears to be predisposed to it. Many observers believe that the disease is due to the action of various toxic agents on the nervous system, and others contend that it is microbic in origin.

Injury to the mouth by dental instruments appeared to be the primary cause in several instances of pemphigus observed by Ormsby, and in a patient with pemphigus under the care of the writer the disease developed immediately following a localized Vincent's infection of the gingival mucosa attributed to dental injury.

Treatment.—There is no specific remedy. Arsenic is of some value in certain cases, and others are benefited temporarily by intravenous injections of quinin or arsphenamin. Autogenous vaccines and autoserum injections have proved useless. The general management of the patient, careful nursing, and the maintenance of a good state of nutrition are of great importance. Much may be accomplished by good hygiene, a nutritious diet, daily baths, and tonic medication with iron, malt and cod-liver oil.

The mouth should be cleansed frequently with a solution of hydrogen peroxid, followed by an alkaline antiseptic mixture or by a solution of potassium permanganate, and iodized phenol may be applied to eroded surfaces. Spraying of the mouth with a weak solution of novocain may subdue pain sufficiently to allow the taking of nourishment, and loosely

attached epithelial shreds and membranous deposits should be removed to prevent them from being aspirated.

Other Dermatoses Producing Lesions in the Mouth

The mucous membranes may participate in the symptomatology of a number of other dermatologic conditions which will require only a brief discussion, inasmuch as their oral lesions are more or less incidental in character or of rare occurrence.

Dermatitis herpetiformis frequently presents lesions on the tongue, lips and cheeks, attended with pronounced sensations of burning pain. They occur in crops as small vesicles at irregular intervals, rupture speedily and form small, bright red, circular or confluent erosions, partly covered with a whitish film. Healing takes place rapidly and without scars.

The disease is persistently recurrent, though often controllable by arsenic given as Fowler's solution. Intramuscular injections of autoserum given repeatedly are of decided value in some cases but ineffective in others. The general condition of the patient should always receive careful attention with especial reference to elimination, nutrition, rest, and general hygiene. A vegetarian diet is sometimes beneficial. Local applications of argyrol or similar salts of silver are often useful for the relief of pain.

Herpes zoster of the mouth, a rare condition, develops acutely with neuralgic pain in the areas supplied by the fifth cranial nerve as a unilateral eruption of clustered vesicles, which may be hemorrhagic. It is a self-limited disease and the treatment is symptomatic, requiring sedatives for the relief of pain and the frequent use of antiseptic mouth washes, with at times local applications of novocain.

Purpura often appears in the mouth as pinhead to nut-sized, bluish red or plum-colored hemorrhagic vesicles or bullæ, or as ecchymotic patches, which develop rapidly and are soon absorbed. The edges and tip of the tongue and the buccal mucosa are frequent sites, probably because of trauma. The treatment is that of the general condition of which the symptoms in the mouth are a part, and the frequent use of mild antiseptic and astringent mouth washes. The application several times daily of a solution composed of equal parts of the tinctures of myrrh, nutgall and krameria is a useful astringent. The use of ice in the mouth should be avoided in this condition because of its possible damaging effects on the capillaries.

Angioneurotic edema frequently affects the mucous membranes and may exhibit a tendency to recur at the same site. The lesions are single or multiple, circumscribed, edematous, transitory swellings of varying size, which may involve the entire lip or tongue, and the faucial or other

regions and produce alarming suffocative attacks. The treatment is essentially that of urticaria. A prolonged course of Carlsbad salts, with daily exercise in the open air, tepid baths, and regulation of the diet has been of most benefit in the writer's experience. Severe attacks are rapidly relieved, though as a rule only temporarily, by the hypodermatic use of a 1:1,000 adrenalin chlorid solution.

Papillomata may develop anywhere in the mouth, but are most common in the faucial regions and on the uvula and palate. They spread rapidly, are usually multiple, flat, and of pinhead to split-pea size. They disappear rapidly after one or two ten-minute exposures to radium on a full strength plaque screened with rubber dam, and at the same time untreated lesions in the vicinity usually disappear spontaneously.

Scleroderma, xeroderma pigmentosum, acanthosis nigricans, mycosis fungoides, epidermolysis bullosa, xanthoma, and verrucæ are other dermatological conditions which rarely present lesions in the mouth and do not require discussion here.[3]

ORAL MANIFESTATIONS OF GENERAL DISEASES

Pellagra.—Pellagra frequently begins with sensations of dryness and burning in the mouth. A diffuse stomatitis often develops early with a peculiar bright reddish yellow color of the mucosæ sharply limited at the mucocutaneous junction, and with superficial ulcerations which bleed readily and are covered with yellowish sloughs. The tongue is swollen and dry, and bright red at the tip and edges where, in severe cases, superficial ulcers form later, covered by yellowish sloughs. In mild cases the tongue may be diffusely reddened, and through loss of the papillæ at the tip and margins denuded or "bald" areas are formed. In long-standing cases ulcers may develop on the gums. Burning and scalding sensations are usually present.

Treatment.—Oral cleanliness is to be maintained by the frequent use of mouth washes of hydrogen peroxid and alkaline antiseptic solutions, and the ulcerations may be painted with solutions of the silver salts.

Scurvy.—Stomatitis, with bleeding and swollen gums, is a prominent feature of infantile and adult scurvy. Early in the disease in children the gums are livid, swollen and often show peridental hemorrhage and petechial spots develop on the frenum of the tongue. In severe cases the gums are spongy, bleed readily and hemorrhagic bullæ or sacs may form in the gum tissue over erupting teeth. When teeth are present an ulcerative type of stomatitis often develops in severe cases of scurvy, the teeth may

[3] The treatment given is the treatment of the local condition. It goes without saying that the underlying general condition should also be cared for.

be loosened and drop out, and maxillary necrosis may occur. Salivation, pain, and intense fetor of the breath are present.

Treatment.—Frequent cleansing of the mouth with solutions of potassium permanganate and hydrogen peroxid is indicated, with applications to the gums of tincture of iodin. A dental surgeon should give appropriate care to the teeth, particularly to their necks and exposed root surfaces.

Leukemia.—In chronic lymphatic leukemia hemorrhage from the gums and petechiæ in the oral mucosa are often observed, with hypertrophy of the lymphoid follicles of the tongue, tonsils and pharynx. Necrosis of the infiltrations may occur later and lead to ulceration, with hemorrhagic gingivitis and loosening of the teeth as further complications. In myeloid leukemia the tendency to necrotic and ulcerative changes is not as marked as in the lymphatic form, though hemorrhages are as frequent. The most pronounced involvement of the mouth is observed in the acute leukemias. Hemorrhagic gingivitis occurs early, and extensive sloughing ulcerations develop rapidly in the mouth and throat and give rise to a horrible fetor.

Treatment.—In the acute leukemias an almost continuous flushing of the mouth with solutions of potassium permanganate, hydrogen peroxid, and antiseptic alkaline mixtures is required to ensure cleanliness and relieve the distress. In less severe cases chemical styptics and thromboplastic agents may be applied locally.

Pernicious anemia may be preceded, sometimes for a year or more, by persistent sensations of scalding or burning referred to the tip and edges of the tongue, which shows no changes other than dryness and a glazed appearance. Wise has described the occurrence of an intermittent superficial glossitis and stomatitis. Superficial ulcerations may develop about the tip and edges of the tongue. Atrophy of the lingual and oral mucosa may occur late in the disease.

In the course of *typhoid fever* superficial ulcerations may be developed in the mouth on the palate, cheeks, lips, gums and tongue; in *diabetes* the mouth is often dry and the tongue large and beefy-red, and in *uremia* excessive dryness of the mouth is common and a stomatitis often develops.

ORAL MANIFESTATIONS OF THE EXANTHEMATA

Variola.—Early in the eruptive stage pinhead-sized, bright red macules appear on the buccal, palatal and faucial mucosæ, become papular, then flatten out into grayish spots and are converted into erosions or small superficial ulcers. In the late stages of severe cases the oral mucosa may be swollen and very painful because of numerous erosions. Lesions may

be present on the tongue, and occasionally a severe glossitis develops with much swelling.

Varicella.—A scant eruption of vesicles on the palate, tongue, buccal mucosa and in the pharynx often accompanies or may precede the cutaneous eruption. The vesicles rupture early and are replaced by erosions with red areolæ.

Scarlet Fever.—The buccal mucosa, the palate and uvula may be swollen and show a punctate hyperemia before the eruption appears on the skin, and white patches on the gums are often present during the first week as the result of epithelial desquamation. Later the soft palate, uvula and fauces are edematous and intensely reddened, and the tonsils may be covered with a pseudomembrane. In severe or septic types ulcers form on the cheeks and gums and an exudate covers the palate and fauces. The oral sepsis is intense, and sloughing and necrosis of the soft palate with perforation may occur. The tongue in scarlet fever is heavily coated at first, but soon assumes the characteristic strawberry appearance due to enlargement of its papillæ and desquamation of the early coating. In severe cases the tongue is intensely reddened and ulcerations may develop upon the margins.

Measles.—During the invasive period of measles, before the cutaneous eruption appears, the fauces are hyperemic, small macules may be present on the palate, and in nearly all cases Koplik's spots are to be seen on the buccal mucosa and inside of the lips. These are small, discrete, irregular, bright red spots, each marked in the center with a minute, bluish white speck. They may be few in number or cover the inside of the cheek and, as the cutaneous eruption develops, the spots are diffused as tiny white dots over the congested mucosa. Aphthous and ulcerated stomatitis may develop in debilitated children, and noma is a rare complication.

Rubella.—Forchheimer has described an eruption of small, discrete, dark red papules which appear early on the soft palate and disappear in from twelve to fourteen hours. Small, discrete, dark red spots without a central white speck are often present on the buccal mucosa. Aphthæ and stomatitis have also been observed.

Treatment.—Frequent cleansing of the mouth and throat with weak antiseptic solutions should be a routine procedure in the nursing care of the exanthemata, both to lessen secondary infection and prevent involvement of the middle ear.[4] When lesions are present mouth washes of hydrogen peroxid and potassium permanganate may be used, with tincture of iodin or silver salts for local application. When oral sepsis is pronounced, frequent and copious irrigations of the mouth, nose and throat

[4] Care of the mouth also prevents parotitis, which has almost disappeared as a complication of infections since adequate care of the mouth has been instituted.—Editor.

with a solution of potassium chlorate are valuable. Other therapeutic measures have been described in the preceding chapter on Oral Sepsis and Stomatitis.

ORAL MANIFESTATIONS OF OTHER INFECTIOUS DISEASES

Leprosy.—Leprosy of the nodular or mixed form involves the lips by extension of the lepromatous infiltration from the adjacent skin, and occurs on the hard and soft palate, uvula, and posterior wall of the pharynx, in infiltrated patches with raised edges, and in nodular masses on the buccal mucosa and the dorsum of the tongue. The lepromata may disappear through absorption or become eroded and later converted into ulcers which heal with deforming cicatrices.

Treatment consists in the use of chaulmoogra oil by intramuscular injection, and of the ethyl esters of chaulmoogra fatty acids.

Foot and Mouth Disease.—This condition when it occurs in man has an incubation period of from two to ten days, followed by mild febrile symptoms, dryness and burning of the mouth, with swelling and congestion of the buccal mucosa. In two or three days, according to Sutton, small superficial vesicles appear on the lips, tongue and in the pharynx, rupture early and form small, tender ulcers which heal rapidly without scarring. In severe forms an erythematous and vesicular eruption appears on the hands and feet, and rarely may be generalized. There is salivation and the regional lymph glands are enlarged and tender.

Treatment is symptomatic. Sutton recommends the use of mild antiseptic and astringent mouth washes, such as solutions of potassium chlorate, alum, and the like, with argyrol as a local application to the lesions.

Rhinoscleroma.—Rhinoscleroma commonly begins in the anterior nares and may extend to the upper lip, gums, palate, and into the throat, as a chronic, slowly advancing infiltration forming tender papules, nodules, and tubercles of cartilaginous hardness. The overlying mucosa is of a brownish or bluish red tint, superficially excoriated or ulcerated at times, and crusted. The teeth may be loosened and fall out of their sockets, and in exceptional cases the soft palate has been perforated. The bacillus described by Frisch and Paltauf is believed to be the causative agent.

Treatment.—In a number of cases radium and X-rays have been successfully used, alone or combined with surgical measures.

Involvement of the mouth may also be present at some time in the course of a number of infectious diseases occurring in tropical countries, such as gangosa, yaws, espundia, verruca peruana, and oriental sore, and in rare instances anthrax and glanders may appear in the mouth.

TUBERCULOSIS

Tuberculosis of the mouth in the great majority of instances develops secondarily to a tuberculous process elsewhere, either through infection with tuberculous sputum or by continuity from lupus of the skin. Infection by way of the blood-stream has not been demonstrated. In the rare instances of primary infection this has developed through contact with a contaminated foreign body, such as dental forceps, or has been attributed to infected raw milk. Tuberculosis of the mouth occurs either as oral lupus vulgaris or more frequently as miliary ulcerative tuberculosis.

In connection with or preceding the cutaneous lesions of lupus vulgaris, grayish or pink, pinhead-sized, soft papules develop on the mucosa, usually in small groups, and by confluence form an elevated, glassy, translucent patch with a pebbled surface. The patches are soft, bleed readily, and may slowly develop into small tumors, or more often undergo necrosis and form irregular, punched out, superficial ulcers with a purulent or granular base. As in lupus of the skin spontaneous healing with dense scar formation may occur. In cases of long standing, nodular patches, small tumors, and ulcers may coexist. Ulceration occurs most frequently in the lesions involving the hard and soft palate, and though usually superficial may result in perforation. The soft, nodular, translucent patches infiltrate the gums, cause the teeth to loosen and drop out, and in the process of healing cicatricial retraction of the gums and fusion with the mucosa of the lip may occur. Lupus of the tongue is exceedingly rare.

The miliary ulcerative form of tuberculosis, the tuberculous ulcer, is found most often on the oral mucous membrane. It may affect any part of the mucosa, either as a small and localized ulcer, or as an extensive ulcerating process. The elementary lesions are gray or yellowish papules, which ulcerate and by coalescence form larger, circular or ovoid ulcers. The edges of the ulcers are polycyclic, abrupt, only slightly undermined, soft, not infiltrated, and are surrounded by a narrow, violaceous zone. The ulcer base is uneven, granular, partly covered with thin pus, and a number of yellow granules or grayish, miliary ulcerations may be present on its floor or on the adjacent mucosa. Tuberculous ulcers are usually shallow, though deep, fissured ulcers may occur. The neighboring lymph glands may be enlarged. Pain is always present and may be severe. The course is slow, prolonged over weeks and months, with almost no tendency to spontaneous healing. In exceptional cases the course is acute, with rapid formation and extension of the ulcers.

The sites of predilection are on the lips, especially the lower lip, tongue, cheeks, and soft palate. When situated in the median line of the lip the ulcer is frequently of the fissured type, and at the commissures may be papillomatous or verrucose. A chancriform ulcer may occur on the

lips, especially in children, with a striking clinical resemblance to the chancre of syphilis, or it may at times resemble an epithelioma. Labial ulcers are extremely painful. The parts of the tongue most often involved are the tip and lateral borders, owing to trauma by sharp edges of teeth. Deeply fissured, painful ulcers develop here and on the dorsum of the tongue, with extensively undermined edges. On the buccal mucosa and soft palate the ulceration tends to be superficial and extensive and may involve the gums.

Treatment.—In addition to the usual climatologic, dietetic, medicinal and other measures employed in the care of the tuberculous patient, local treatment of the lesions is required. In lupus of the mucosa local treatment alone often suffices, though general measures are always of benefit. In patients with far-advanced pulmonary tuberculosis, relief of pain may be all that can be attempted, and for this cocain and iodoform in oil are of value. In other cases local measures which are destructive to the infected tissues are indicated. These include the use of radium, X-rays, the actual cautery, fulguration, diathermy, ultraviolet light, lactic acid, and trichloracetic acid, and the choice of the agent is to be determined by the location and extent of the tuberculous process. Surgical excision is not advisable unless the cautery knife is used.

SYPHILIS

Syphilis of the mouth is of frequent occurrence. With some exceptions the lesions are counterparts of the cutaneous manifestations of syphilis, modified by structural differences in the affected tissues and by the influence of warmth and moisture, local irritation, and secondary infection.

Chancre.—Chancre of the mouth is the most common of the extragenital chancres, and occurs with greatest frequency on the lips, usually the lower lip, less often on the tongue and tonsils, and only exceptionally on the gums or buccal mucosa. It is usually single, but may be multiple. The chancre may appear as an erosion, small ulcer, or eroded papule, with a red, moist surface from which a clear serum, containing spirochetes, oozes more or less freely. It is painless, indolent, and gradually acquires a dense infiltration at its base.

Chancre of the lip when fully developed is usually a dense inflammatory mass of considerable size and of cartilaginous hardness at the base, causing the lip to protrude and be partially everted. The surface is eroded or covered by a thin pellicle, bleeds readily, and may be covered by an adherent crust on its cutaneous portion. The adjacent mucous membrane is tumified, dry, scaly, and often fissured. While the lesion just described is the usual type of labial chancre, this may also occur as a small, ulcerated papule or large ulcerated mass. Attending the chancre is an indolent,

firm, often unusually large swelling of the lymph glands beneath the jaw and, when the chancre is on the upper lip, of the preauricular glands on both sides.

Chancre of the tongue usually occurs on the dorsum near the tip as a large, excavated ulcer, with a firm barrierlike margin, and is attended by lymphangitis, with considerable swelling of the surrounding tissues. Chancre of the gum is rare and occurs most often as an eroded induration about the roots of one or more teeth. Chancre of the buccal mucosa is likewise rare and has no unusual or distinguishing characteristics. When the tonsil is the site of chancre it is usually enlarged in its entirety, and the surface is covered by a dense, tightly adherent false membrane beneath which the tissues are eroded or ulcerated to a variable depth. The involved area is firm and indurated, all the tissues in the vicinity are densely swollen, and the regional lymph glands are firm and tumefied. It is practically always unilateral.

Secondary Syphilis.—The most frequent of all lesions of syphilis that appear in the oral cavity are the mucous patches or erosive plaques. They occur most often in the first six or eight months after infection, tend to relapse, and may recur during a period of several years. In number they may be few or many, and the sites of predilection are the half arches, the sides, tip, and under surface of the tongue, the buccal mucosa near the angles of the mouth, the surface of the tonsils, and the anterior part of the floor of the mouth, though no part of the mouth or pharynx is exempt from their presence. Mucous patches occur in the mouth either as macular syphilids or erosive or ulcerated papules. The macular type is a transitory, generalized symmetrical redness of the velum and anterior pillars of the fauces, occurring early in the eruptive stage, and usually accompanies the mucous papule of the erosive type, which is the form most often assumed. This is a syphilitic papule in which, through shedding of the superficial epithelium, the deeper layers are exposed and exudation occurs. Clinically they are eroded or superficially ulcerated areas, circular or oval in shape, with a diameter of from 2 to 20 mm., and are usually covered by a thin shred of macerated epidermis and exudate of a gray or yellow color. This pellicle is often adherent and on its removal a bleeding, bright red surface is seen. The lesions have well-defined, nonelevated margins, are surrounded by a narrow bright red areola and, though usually discrete, several patches may touch at their margins and coalesce, forming polycyclic or irregularly contoured lesions. In this manner large areas of the mucosa, especially on the gums or floor of the mouth, may be eroded and form one large mucous patch. If infection occurs the surface may secrete a thin puriform fluid, the surrounding areola extends and becomes more inflammatory, and the lesions may ulcerate. The surface of the lesion is flat and slightly depressed, or exceptionally elevated, and an infrequent type of mucous patch occurs at

the commissure of the lips in which the surface becomes hypertrophic and forms a vegetating, cauliflowerlike mass or condyloma.

The ulcerated syphilid as it occurs in the mouth may be superficial or deep, single or multiple, rounded or irregular. The deeper types are usually seen about the fauces or tonsils. Their edges are raised, sharply cut, the bases are smooth, not hard, and red or yellow in color, and exude pus. When situated at the angle of the mouth they are usually deeply fissured and painful, with the appearance of a scald.

When located on the dorsum of the tongue the mucous patch usually causes loss of the papillæ, and forms an irregular, smooth, polished, deep pink, slightly painful lesion of finger-nail size. Several such patches are present as a rule, and by coalescence with neighboring lesions may involve almost the entire dorsum of the tongue, producing the condition known as the *smooth glossitis* of early syphilis.

Tertiary Syphilis.—Gummata and interstitial infiltrations represent the lesions of late syphilis of the mouth. Gummata in the mouth do not differ clinically from gummata elsewhere, involve both the soft and osseous structures, and may cause extensive destruction. They occur most often on the palate, dorsum of the tongue, and in the tonsillar region and pharynx as painless, usually single tumors which involute and disappear or break down into deep and destructive ulcers. The soft palate is a site favored by the gummatous, rapidly destructive ulcer, which usually begins as a diffuse inflammatory, almost painless thickening of the velum, soon followed by rapid ulceration and phagadena with perforation and extensive necrosis, at times involving the pharynx. Periosteal gummata occur on the hard palate in the median line, become necrotic and cause perforation. Gummata of the tonsil often are rapidly destructive, while those of the pharynx tend to be indolent and cause relatively little destruction. Gummata of the tongue occur usually on the dorsum as single or multiple, firm, painless nodes situated deep in the body of the tongue. When single the gumma often breaks down into a deep crateriform ulcer, whereas multiple gummata tend to resolve and produce fibrosis of the tongue.

Interstitial syphilitic infiltration of a sclerogummatous type met with in the viscera is frequent in the tongue and may also occur in the lips where it produces an elephantiasic condition (macrocheilia). In the tongue the process usually is slow and insidious, and results in a clinical picture that varies with the extent, depth and stage of the process.

Sclerosis of the Tongue.—When the infiltration is diffuse and deep, the tongue early in the process is enlarged and stiff, later becoming smaller, hard and rigid, the papillæ are lost and the surface assumes a smooth, red, tense and shiny appearance. Superficial furrows are present early and grow deeper as sclerosis progresses, and as a result of unequal contraction the tongue becomes nodular, lobulated, crumpled, concave or

otherwise deformed. Ulceration may occur, usually as the result of injury, and is slow to heal.

Smooth Atrophy of the Tongue.—Interstitial infiltration when it is diffuse and superficial produces a condition similar to that of the sclerosis described above, without the symptoms due to contraction and atrophy of deep infiltration. A diffuse or patchy smoothness of part or all of the dorsum of the tongue is present, with superficial furrowing and some distortion. The condition often is confined to the base of the tongue behind the circumvallate papillæ and is readily overlooked.

Macroglossia may be produced by lymphatic obstruction due to syphilitic lymphangitis or to secondary infection of syphilitic lesions.

Treatment.—The treatment of syphilis of the mouth does not differ from the treatment of syphilis in general. The response of lesions of the mucous membranes to arsphenamin, mercury and the iodids is as pronounced as that of lesions occurring elsewhere and, owing perhaps to greater vascularity of the parts, involution due to treatment may be even more rapid. Frequent cleansing of the mouth with solutions of hydrogen peroxid, potassium chlorate, and various antiseptics is essential, and solutions of silver salts may be applied directly to the lesions. The use of caustic agents is not advisable, and irritant or highly spiced articles of food and tobacco should be interdicted. Gummas should never be incised nor excised, and the only indication for surgery is the removal of bony sequestra. Plastic surgery may be required to remedy the defects produced by gummatous processes, especially in the palate, after the process has become inactive.

Leukoplakia

Leukoplakia of the mouth is discussed here in connection with syphilis, not because it is a syphilitic process in itself, but because of its frequent occurrence on a syphilitic basis. Leukoplakia is a chronic disorder of the mucous membranes, most often of the mouth, characterized by the development of one or more, smooth, thick, gray or white patches, which tend to persist. It is seen in males with greater frequency and occurs chiefly during and after middle life.

Etiology.—Leukoplakia of the mouth is the most frequent form of keratosis or increased cornification of the mucous membranes, and is due to chronic inflammatory changes induced in response to chronic irritation of varied origin. Tobacco is a frequent cause, and malocclusion of the teeth, nervous mouth habits, habitual ingestion of hot foods and fluids, abuse of condiments and alcohol, and ill-fitting dental appliances may all be concerned in its production, acting together with perhaps an individual tendency to hyperkeratosis in response to irritation. Leukoplakia

frequently, but by no means invariably, develops on a mucous surface that has been structurally altered by previous syphilis. Quoting Pusey:

"Even in syphilis leukoplakia is rarely a manifestation of syphilis itself; it is only so in rare cases in which there is a proliferation of the epithelium over an area of active syphilitic manifestation which has not yet disappeared."

Symptoms.—Leukoplakia of the mouth appears chiefly on the dorsum and edges of the tongue, on the interdental surface of the buccal mucosa, especially near the angles of the mouth, on the gums above the upper lateral incisor and canine teeth, on the lateral and posterior surface of the hard palate, and on the inner and vermilion surface of the lips. Other parts of the oral surface are less often affected and the disorder is rarely seen in the pharynx.

The mucosa of the affected region gradually loses its transparency, grows hazy and opaline or may become reddened, and one or more grayish or whitish, opaque patches of varying size and configuration appear. These patches may be sharply outlined or merge gradually into the normal mucosa, are without palpable density or only slightly thickened, and by confluence form striated, variegated, or checkered designs. Exfoliation in small shreds may occur, especially from the surface of the interdental space of the buccal mucosa and from the inner surface of the lips. The process may become stationary at this stage or it may progress with the gradual development after months or even years of thick, angular, or rounded, white patches, which often are elevated sharply above the adjacent reddened and tender mucosa, and are rough, hard and inelastic to the touch. The patches are closely adherent and may exceptionally become detached as a whole or in part, but recur rapidly. Deep furrows and fissures develop and the latter may extend to the corium; at times keratotic or warty projections and nodules form on the surface.

Darier has called attention to chronic ulcerations observed in leukoplakic patches on the tongue, cheeks and lips, which he ascribes to a local nutritional disturbance of the mucosa referable to an underlying sclerosis and arteritis, or, in other words, they are trophic ulcers. Darier describes them as being "irregular, often angular in shape, with a bright red, smooth or finely mammillated floor. The floor is frequently raised to a level with the borders from which it is separated by a deep, sharply cut-out furrow that is brought into view by unfolding it." The leukoplakic ulcer resists treatment, tends to recur, and does not have the marked potentiality for malignant change that is found in the warty forms and deep fissures of leukoplakia.

Leukoplakia of syphilitic origin, except as it involves the tongue, cannot be differentiated clinically from non-syphilitic leukoplakia. When,

however, lesions such as are described above occur on the tongue in association with red, glistening, polished areas, or other areas in which the surface is eroded or ulcerated, and when the tissues of the tongue are thickened by inflammation, the diagnosis of syphilitic leukoplakia can be made. The polymorphic character of the process is a distinguishing feature, and although the lesions differ in clinical appearance they are developed on the same pathologic basis.

The *subjective symptoms* consist of sensations of dryness and stiffness, with at times tenderness of the mucosa in the vicinity of the leukoplakic patches. Frequently the patient is not aware of the presence of extensive leukoplakic changes. Thick, rough, and verrucous patches, through their rasplike contact with opposed mucous surfaces, may act as local irritants and become irritated and tender themselves. Pain, often of a shooting or radiating character, occurs when deep fissures are present, and may be indicative of an epitheliomatous change.

Treatment.—It is the general belief in this country that antisyphilitic treatment for leukoplakia is useless, inclusive of that occurring in the syphilitic. A belief directly opposed to this, however, is held by many who claim that under antisyphilitic treatment some leukoplakic patches disappear permanently or temporarily and that the process may be arrested. Darier is an advocate of arsphenamin and mercury when leukoplakia occurs in the syphilitic, and in addition employs local injections of dilute cyanid of mercury. He does not recommend the use of iodids. When the histopathology of the leukoplakic process as it occurs in syphilis is considered, a specific action from the use of arsphenamin and mercury can be expected only in exceptional instances. However, in the presence of leukoplakia in an evident syphilitic, specific treatment should be instituted or withheld only after due consideration of the therapeutic requirements of the individual in general and not of the tongue or mouth alone.

The general state of health should be investigated, especially in regard to digestion and elimination. The use of tobacco, hot foods and drink, condiments, alcohol, and pungent dentrifices must be avoided. Rough and sharp teeth should be ground smooth, and carious or broken teeth extracted or repaired by a competent dentist, who also should investigate the condition of crowns, bridgework or plates. The strict maintenance of oral cleanliness is of great importance and mildly astringent and alkaline mouth washes should be used frequently.

The local use of balsam of Peru, salicylic acid, resorcin, methylene-blue, silver nitrate and other agents has been advocated, with chromic acid, acid nitrate of mercury, lactic acid, carbon dioxid snow, and the like, for their destructive action in thickened patches. A word of caution appears advisable here against the use of any measure in leukoplakia that is not thoroughly and powerfully destructive. It is the opinion of the

writer based on experience that the use of such caustics as silver nitrate, lactic acid, carbon dioxid snow, and other like agents is meddlesome and dangerous. Electrolysis is advocated by Corlett as superior to all other measures of treatment. The actual cautery at red heat and the cautery knife are at present the most effective and reliable agents for the destruction of deep and thickened patches. Radium has been successfully used in leukoplakia, but should be employed only by an expert. It is especially effective in the treatment of superficial and thin patches, though with proper filtration and dosage deep lesions may likewise be attacked with radium. The use of X-rays in leukoplakia has been abandoned. If an epithelioma develops, surgical procedures for its immediate removal are indicated.

The treatment of leukoplasic ulcers according to Darier consists of vigorous antisyphilitic treatment, local mercurial injections, proper oral hygiene, care of the teeth, and the use of radium or X-rays. Caustics are to be avoided.

DISEASES OF THE MOUTH DUE TO FUNGI

Actinomycosis.—The mouth is frequently the portal of entry for the actinomyces fungus, but actual lesions of the disease are uncommon in the mouth. The lips, cheeks, and tongue may be the site of nodular or gummous formations which soften and break down with the discharge of a bloody and purulent fluid containing yellow granules composed of fungi. Dense scar formation may occur. In the jaw the disease occurs as a periostitis.

Treatment.—This consists in surgical removal, deep cauterization, or curetting of the diseased tissue, and in the administration of potassium iodid in large doses for a period of months. Copper sulphate used internally in a dose of ½ to 1 gr. three times a day, and in 1 per cent solution for irrigation, is often beneficial. Treatment with X-rays is of great value and in the writer's opinion should be used in every case, conjointly with potassium iodid or copper sulphate.

Monilia candida.—The infection due to this fungus has been described by Engman and Weiss. The entire buccal mucosa of one side and the hard palate were covered with a thickened, fissured, sharply defined mat of white and glistening filiform projections on a whitish, macerated base, with an appearance like that of a "frozen doormat." A fungus identified as the Monilia candida was constantly found firmly engrafted on the lesion. The condition had existed for several years, resisted local treatment including cauterization, and carcinoma finally developed.

Blastomycosis.—Blastomycosis rarely invades the mouth. Vegetative tumors may develop on the lips, and in two recorded cases there were

nodular tumors at the base of the tongue. In systemic blastomycosis abscess formation has occurred in the pharynx. The *treatment* consists in the use of large doses of potassium iodid, and X-rays or radium. Curetting of the lesions is followed by recurrence.

Sporotrichosis.—Sporotrichosis when it occurs in the mouth forms exuberant, grayish yellow ulcers, which are not covered by a false membrane. They tend to extend on the surface rather than deeply and are not as destructive as tuberculous or syphilitic ulcers of the mucosa. In exceptional cases the ulcers of sporotrichosis may involve the base of the tongue and extend to the larynx and trachea.

Treatment.—Potassium iodid is a specific in this disease and should be given in full dosage and continued for several weeks after the lesions have disappeared. If nodules are present they should not be incised because open lesions respond less readily to treatment than others. Mouth washes containing iodin may be used.

DISEASES OF THE TONGUE

The diseases of the tongue that have been discussed in preceding chapters are such as occur in the course of disease processes affecting the mouth in general and in which involvement of the tongue is a coincident feature. In this chapter several other disorders, chiefly inflammatory, that are confined to the tongue, will be considered.

Geographical Tongue.—Geographical tongue (glossitis areata exfoliativa, erythema migrans, wandering rash, transitory benign plaques, exfoliatio areata linguæ) is a chronic, recurring, inflammatory disease of the tongue, characterized by the presence of superficial circinate patches which undergo rapid variation in shape and size.

It occurs in both sexes and is said to be most common in children. In the writer's experience it has been seen most often in adults and chiefly in women. The writer found the geographical tongue in 20 out of 2,980 drafted men who appeared before a medical advisory board.

The disease begins as one or more, small, whitish or yellowish patches on the dorsum or borders of the tongue. They enlarge rapidly by peripheral extension, while the central portion desquamates and becomes smooth and beefy red in color, the redness being more pronounced toward the margin of the lesion. Oval and circular lesions are formed, with soft, narrow, slightly raised, irregularly convoluted borders of a characteristic grayish yellow or sulphur yellow color. The filiform papillæ within the red central area are often shed, and the fungiform papillæ thereby acquire an added prominence. The lesions enlarge rapidly and by confluence with neighboring lesions the borders are broken up into segments of circles and form continually varying, polycyclic designs. The outer border of the

design continues to advance, while the included segments are rapidly lost in the central desquamation. Concentric rings are sometimes formed.

Individual patches may last for seven or ten days and then disappear without a trace, but the process usually is continuous and, except during short intermissions, one or more lesions in various stages of development are always present. The affection lasts for years or indefinitely and produces no subjective symptoms except slight itching or pain due to irritation by foods or drink. A transitory superficial glossitis may rarely be present.

Etiology.—Its etiology is unknown. It has been regarded as of parasitic origin, although no related fungus has ever been found, and seborrhea and the "exudative diathesis" have been suggested as etiologic factors. The condition bears no relation whatever to syphilis, but owing to an incorrect diagnosis may unfortunately give rise to a syphilophobia. Furrowed or sulcated tongues are predisposed to the disorder. It is not contagious, though it may be familial, and the writer has seen the condition in twin boys. The histopathology is that of a subacute inflammatory process of the mucous membrane of the tongue.

Treatment.—The disease is resistant to treatment. It occurs usually in apparently healthy individuals, and dietary regulations are not required other than that nuts, cheese, condiments, hard breads, and excessively hot foods and drink should be avoided because they often act as irritants. Associated gastro-intestinal disorders should be given attention. Alkalis such as calcined magnesia and sodium bicarbonate have been beneficial in some cases, and arsenic has been recommended. Locally, astringent and antiseptic mouth washes and applications of 2 per cent chromic acid may be used. The teeth should be put into good condition and attention given to oral hygiene. Short, repeated exposures of the lesions to radium are recommended by Ormsby as curative.

Moeller's Glossitis or Chronic Superficial Excoriation of the Tongue.—Moeller's glossitis is a chronic inflammatory disorder of the tongue, characterized by the presence of multiple, red, smooth, irregular, intensely painful patches. It is an uncommon disease and occurs only in adults, chiefly women, of middle life. The lesions are irregular, more elongated than rounded, sharply defined, intensely red patches with an excoriated or "brush-burn" appearance. They are not elevated, depressed, or indurated, show only slight tendency to lateral extension, and generally retain their original size and outline without much change for weeks or months. The epithelium of the patches is thinned or lost through desquamation, the filiform papillæ are thinned or absent, and the fungiform papillæ are hyperemic, swollen, and often give a stippled appearance to the patches. The tip and borders of the tongue are the sites of predilection, though lesions may appear on the gums, cheeks, palate and lips. Ulceration never occurs.

The disease pursues a chronic course with periods of exacerbation and of lessened intensity at irregular intervals. Pain is always a prominent feature, and is usually constant and burning in character, though it may be paroxysmal and lancinating. It is often of such intensity as to prevent the taking of food, and in a patient seen by the writer it interfered with sleep. The pain is increased on irritation produced by hot, coarse or highly spiced foods, extremes of temperature, and pressure against the teeth, and the sense of taste is often diminished. Loss of weight usually occurs, and, harassed by constant pain for which no relief is obtained, the patient may become melancholic or hysterically desperate.

The *cause* of Moeller's glossitis is unknown. The presence of tapeworm has been recorded in 7 cases, but Harris regards this as coincidental. Engman and Weiss suggest that apical abscesses and pyorrhea may have been the etiologic factors in their case.

Treatment.—The disease persists as a rule in spite of treatment and complete recovery is exceptional. Sodium bicarbonate in large doses has given relief in some cases, and others have been benefited temporarily by lactic acid bacilli. Anthelmintic treatment has been followed by cure or improvement in several instances. In the patient of Engman and Weiss recovery occurred after the removal of two infected teeth and the disappearance of a pyorrhea. Locally, the alkaline antiseptic solution (N. F.) is often soothing, at least for a time, and may be used alternately with other similar mild mouth washes. Two per cent zinc sulphate solution and milk of magnesia may give relief in some cases, and a dressing of parresine as used for burns may be tried. Nuts, cheese, chocolate, the acid fruits, and all condiments act as irritants and are to be avoided, and the patient soon learns that food of a certain consistency and temperature is least irritating. Infected teeth, gums, and tonsils should receive appropriate dental and surgical treatment. It is important to maintain a good state of nutrition and general health by hygienic living, nourishing food, and tonic medication.

Papillitis Lingualis.—Papillitis lingualis, described by Duplaix in 1893, is an uncommon affection of the tongue, in which desquamation of the epidermis occurs and involves only individual papillæ. According to Harris, small points of intense red, hidden in the folds of the mucosa, and visible only with a lens, are found on the tip and borders of the tongue. They are intensely painful and have an appearance as if a small piece of the mucous membrane had been punched out. The only complaint is that of pain, which is severe, burning and often neuralgic in character, and interferes greatly with eating.

Treatment consists in touching the painful spots with the galvanocautery.

Acute Diffuse Glossitis.—This uncommon condition usually occurs in severe forms of stomatitis and may be present in erysipelas, scarlet fever,

typhoid fever, and small-pox, and in the latter disease is always an unfavorable sign. It may also be traumatic in origin.

An inflammatory, diffuse or unilateral swelling of the tongue develops rapidly, attended by severe pain, salivation, enlargement of the neighboring glands, and fever. The swelling may reach such dimensions that the tongue hangs out of the mouth, and abscesses and superficial ulcerations may develop. Streptococcic infections may be rapidly fatal. Supportive measures and the local use of ice and antiseptic mouth washes are indicated, with early and deep longitudinal incisions in the severe cases.

Glossodynia Exfoliativa.—Under the name "glossodynia exfoliativa" a chronic, recurrent form of superficial glossitis has been described in which bright red streaks or patches, with prominent papillæ, are formed through an exfoliation of the corneous layers. It generally occurs in poorly nourished women, and burning pain, often of great severity, is present.

Treatment is not successful. It is not unlikely that many of the cases are examples of Moeller's glossitis.

Various other inflammatory conditions of the tongue, accompanied by pain of more or less severity, have been described. Extension of a lingual tonsillitis to involve the papilla found at the junction of the palatoglossal fold with the tongue on either side may be the cause of protracted pain extending into the tip of the tongue. Engman thinks the condition of "burning tongue" described by him may be due to this cause. Glossitis papillaris is an inflammation limited to the circumvallate papillæ, attended by a sensation of burning, cough, and more or less dysphagia.

Pneumococcus infection of the tongue has been described by Engman and Weiss, with the formation of raised, white, circinate patches, either furry or smooth, on the tongue, hard palate and buccal mucosa. Cultures gave an almost pure growth of pneumococci. In another, though culturally undetermined case, there was a serpiginous eruption of minute papules on the tongue, with soreness, of several months' duration, which rapidly disappeared in response to local applications of a saturated, aqueous solution of oxgall.

The writer has repeatedly observed, but has not seen described, an inflammation localized to the vertical plications of the mucosa on either side of the base of the tongue, which occurs not infrequently as the result of irritation due most often to certain foods, especially nuts, pungent cheese, and chocolate. There is swelling, redness and tenderness, generally limited to one side, with sensations of soreness or moderate pain referred to the side of the tongue. The condition often persists for weeks or months, but subsides rapidly upon removal of the cause.

Median Rhomboidal Glossitis.—Median rhomboidal glossitis is an affection described by Brocq and Pautrier, which occurs on the dorsum

of the tongue immediately in front of the circumvallate papillæ, as an oval or rhomboidal, reddish, denuded-looking, well-defined patch. The lesion is smooth or more often granular and mammillated, slightly indurated, painless, and persists for years without change. The histopathology is that of chronic inflammation with infiltration and sclerosis. The condition is not uncommon, occurs chiefly in adults, is of unknown etiology, and has thus far resisted all local or general treatment.

Glossodynia.—Glossodynia, or pain in the tongue without glossitis or other discernible lesion, is occasionally encountered in hysteria, in the insane, and in tabes where it corresponds to the crises observed in other organs. The pain is usually referred to the tip and borders of the tongue, occurs in paroxysms, and may be intense. Lingual neuralgia is most often unilateral and there is tenderness of the lingual nerve.

Involvement of the tongue in angioneurotic edema, pellagra, purpura, pernicious anemia, and other diseases has been discussed in the preceding pages.

Black or Hairy Tongue.—The hairy black tongue, or lingua nigra, is produced as the result of an hypertrophy of the corneal sheaths of the filiform papillæ, which become elongated, assume a brownish or black color, and resemble a patch of hair. The patch develops gradually or rapidly, beginning in the midline of the tongue usually anterior to the circumvallate papillæ, then extends forward and may cover a large portion of the dorsum. The papillæ or "hairs" may attain a length of 1 cm. or more, and are darker toward the tip. The discoloration is probably due to the presence of chromogenic bacteria. The patches are thick and furlike, darkest in the center and fade to a light brown toward the margins. After persisting for several months or even years, the patches disappear by a gradual desquamation of the epithelium; recurrence is frequent. The disorder is benign, not contagious, and occurs mostly in adults and the aged. Investigation has failed to establish the suspected parasitic origin of black tongue, and the etiology remains obscure.

Treatment has been unsatisfactory. The use of alkaline mouth washes for oral cleanliness, and the avoidance of tobacco and irritant foods are advisable. The patches may be painted with a 2 or 5 per cent solution of salicylic acid; lactic, chromic, and trichloracetic acid have also been employed. Scraping or curetting is followed by recurrence.

Aspergillus Infection.—Aspergillus infection of the tongue is extremely rare. The writer has seen one case, by the courtesy of Dr. R. S. Hopkinson, which was clinically indistinguishable from black hairy tongue. The entire dorsum of the tongue was covered with a matted, furlike, slimy, black patch of hairlike filaments, the color changing to brown toward the margins. When scraped there was slight bleeding from the base. The Aspergillus nigrescens was found in abundance. In Winfield's patient there were edematous patches on the hard and soft palate,

covered with a firmly attached, yellow deposit. Applications of a 25 per cent ethereal solution of hydrogen peroxid removed the lesions.

Sprue.—In sprue or psilosis, a chronic, relapsing tropical disease, sore mouth and tongue, diarrhea and anemia are the cardinal symptoms. Vesicles, erosions, and small ulcers develop at intervals on the tongue and oral mucosa, with moderate salivation. The tongue assumes a pink color, is flabby, the fungiform papillæ are enlarged and hyperemic, and during remissions the tongue appears atrophied.

Treatment is essentially dietetic and hygienic. A milk diet, with the gradual addition of eggs, fruit, and fresh vegetables low in carbohydrate content is advocated by Ashford. Wood gives preference to a similar dietary in which milk is replaced by beef. Beneficial effects are also ascribed to the use of a strawberry diet.

Scrotal Tongue.—Sulcated, grooved or scrotal tongue (lingua plicata) is a congenital, often familial, malformation. It is frequently seen in a mild form in ichthyotic individuals and in those with congenital keratoderma of the palms and soles. [5] In well-developed cases the tongue is enlarged, soft, lobulated, and more or less deeply furrowed or fissured. In the folds of the mucosa the papillæ are small or absent, and those on the surface of the tongue may be enlarged. The lesions of geographical tongue in a mild or rudimentary form are often present, and a superficial glossitis may develop through irritation by food and detritus which lodges in the sulci.

Treatment.—Scrotal tongue is a deformity and cannot be influenced by treatment, though it is advisable that the tongue be kept clean by alkaline mouth washes, with swabbing of the deeper sulci.

Xerostomia.—Xerostomia is a persistent dry condition of the mouth, most common in women, due to a diminution or suppression of the salivary and mucous secretions. The tongue and oral mucosa are red, dry, and glazed, the lips are scaly, and the tongue may be painful and fissured. Atrophy of the parotid and submaxillary glands may be present, or the parotid glands may be enlarged.

Treatment.—Xerostomia is resistant to treatment. Galvanism and pilocarpin have been used but are of doubtful value.

REFERENCES

Brocq and Pautrier. Ann. de dermat. et syph., Series 5, v, 1, 1914.
Brown, G. V. I. Oral Diseases and Malformations, 2d ed., 174, 1917.
Butlin. Diseases of the Tongue, 2d ed., 109, 1900.
Campbell and Dyas. Journ. Am. Med. Ass., lxviii, 1596, June 2, 1917.
Darier-Pollitzer. Textbook of Dermatology, 307, 1920.

[5] It is common in mongoloid idiots.—Editor.

Engman and Weiss. Arch. of Dermat. & Syph., i, 119, Feb., 1920.
Fineman. Journ. Infect. Dis., xxviii, 185, 1921.
Greeley. Am. Journ. Med. Sc., clv., 742, May, 1918.
Harris. Journ. Cutan. Dis., xxxiii, 742, 1915.
Hench and Aldrich. Journ. Am. Med. Ass. lxxix, 1409, 1922; editorial, 1769, Nov. 18, 1922.
Hunter. Pernicious Anemia, London, 1901.
Kundratitz. Wien. klin. Wchnschr., xxxv, 624, 1922.
Lane, J. E. Journ. Am. Med. Ass., lxix, 192, 1917.
Lewandowsky. Tuberkulose der Haut, Enzykl. d. klin. Med., 1916. A valuable monograph which has been freely consulted in the preparation of the chapter on Tuberculosis of the Mouth.
Lipschuetz. Arch. f. Dermat. u. Syph., cxxxvi, 428, 1921.
Loblowitz. Ibid., cii, 191, 1910.
Margolies and Weidman. Arch. of Dermat. & Syph., iii, 723, 1921.
McKinstry. Brit. Med. Journ., i, 421, 1917.
Mook. Journ. Cutan. Dis., xxxiii, 667, 1915.
Ormsby. Personal Communication.
Pusey. Journ. Am. Med. Ass., lxxix, 1288, 1922.
Rosenow and Meissner. Ibid., lxxviii, 266, 1922.
Sluder. Am. Journ. Med. Sc., clvi, 248, 1918.
Stevens and Johnson. Am. Journ. Dis. Child., xxiv, 526, 1922.
Sutton. Journ. Cutan. Dis., xxix, 65, 1911; xxxvi, 579, 1918.
——— Journ. Med. Research, xxix, 489, 1914.
——— Diseases of the Skin, 4th ed., 379, 1921; 1083, 1922.
Warfield. Am. Journ. Med. Sc., cxliv, 647, 1912.
Welch and Schamberg. Acute Contagious Diseases, 1905.
Widowitz. München. med. Wchnschr., lxviii, 871, 1921.
Winfield. Journ. Cutan. and Genito-urin. Dis., Jan., 1897.

CHAPTER XXVI

DISEASES OF THE SALIVARY GLANDS

C. P. Howard

DISTURBANCES OF SECRETION

Salivation (*Ptyalism, Sialosis, Sialorrhea*).—One must distinguish a false from a true salivation; in the former, owing to paralysis of the lips, tongue or pharynx or an inflammation of the throat as in tonsillitis and quinsy, there is a constant dribbling or an accumulation of the saliva in the throat because of the absence of the normal swallowing reflex. In true salivation the amount of saliva is increased above the normal limits of 1,000 to 1,500 c.c. per diem; indeed there are records of the excretion of 3 to 4 liters, and even in one case of 11 liters in the twenty-four hours.

According to Kraus, true salivation may be due to a variety of conditions: (1) an idiopathic form in nurslings and in anemia; (2) a cerebral form with irritation of the trigeminal nerve, as in tic douloureux; (3) disease of the middle ear with irritation of the chorda tympani; (4) the sympathetic and reflex form in pregnancy and lactation and in nasal, gastro-intestinal and uterine disease; (5) the nervous and mental affections of rabies, hysteria, idiocy and cretinism; (6) the use of such drugs as mercury, iodid, jaborandi, muscarin and tobacco; (7) pancreatic tumor and occasionally pancreatitis; (8) the acute fevers such as variola; and (9) the sympatheticotonic types of exophthalmic goiter. The symptoms are disturbance of taste, indistinctness of speech, mild dyspepsia with rarely vomiting and diminished urinary secretion.

Treatment.—The first requisite is care of the underlying cause in both the false and the true forms. In addition a mild saline cathartic such as sodium phosphate (2 drams) or Rochelle salts (2 drams) or Epsom salts (2 drams) each morning before breakfast is helpful. Rinsing of the mouth with potassium chlorate (5 per cent), zinc chlorid (1 per cent) or alum sulphate (1 per cent) or the sucking, at frequent intervals, of the official lozenge of potassium chlorate further aids. Of temporary benefit is the hypodermic injection of atropin sulphate (1/100 gr.) or the internal administration of the tincture of belladonna (10 minims) and bromids or opium in full doses.

Aptyalia (*Oligosialia, Xerostomia or Dry Mouth*).—This condition, as the name implies, is due to a diminished secretion of saliva as may occur following the use of certain drugs such as belladonna, atropin, opium and morphin or in certain dehydrating diseases such as fevers, diabetes, Asiatic cholera and in chronic Bright's disease. Jonathan Hutchinson has also described a group of cases in elderly women in poor health in whom the tongue is dry, glazed and fissured, or even wrinkled with atrophy of the filiform and hypertrophy of the fungiform papillæ; although the salivary glands appear normal there is almost complete loss of secretion in this type of xerostomia.

Treatment.—This is even more unsatisfactory than that of salivation; it of course implies care of the underlying condition in the more acute forms. In the chronic types of the disease, all carious teeth should be removed and the patient provided with proper fitting dentures and so prevent the air-drying of the buccal mucous membrane. A simple glycerin mouth wash should be ordered. Internally, jaborandi in doses of from 30 to 40 minims of the official B. P. tincture or a tablet of pilocarpin hydrochlorate (gr. 1/12) on the tongue three times daily may be tried, but with caution. The application of the galvanic or faradic current to the parotid region has been recommended by some.

INFLAMMATION OF THE GLANDS AND DUCTS

Acute Secondary Inflammation.—The primary acute inflammation or mumps is considered elsewhere; we are here concerned only with the so-called secondary or symptomatic salivary gland inflammation. For years this group was spoken of as "sympathetic" "reflex" and "metastatic" owing to ignorance of the underlying pathology. While space will not permit of a detailed enumeration of the various causes of this group, we must mention such local causes as obstruction of the duct and extension of infection from the mouth, and such general causes as abdominal infections and operations and the various infectious fevers and pyemia as typhoid, typhus, small-pox, pneumonia, dysentery, epidemic encephalitis, etc. In the latter group there is reason to believe that the infective agent may reach the salivary gland either by the duct or through the blood-stream. No doubt the lowered resistance of the patient and the diminished secretion of saliva which are present in the above diseases are strong contributory factors. It is noteworthy that the submaxillary and sublingual salivary glands are practically immune to this type of inflammation; this immunity may be due to the mucous secretion of these glands as mucin inhibits bacterial growth. The greater susceptibility of the parotid is also explained by the presence in the salivary gland of lymphoid tissue which of course favors the invasion and development of bacteria.

The symptoms are, briefly, fever, chilliness, or even an actual rigor and vomiting. Locally, there are pain and swelling of one or more of the salivary glands, though most frequently of the parotid. By the third to the fifth day the skin over the affected gland is hot, reddened and tense; there may be marked induration and even fluctuation. Dysphagia, tinnitus or even deafness may occur as a result of pressure.

Treatment.—Surgeons, as well as physicians, have learned to recognize the seriousness of parotitis and are exercising proper prophylactic care of the mouth before major operations and during the course of all acute diseases. The regular use of mouth washes and the sponging and cleansing of the teeth and gums with a mild antiseptic preparation after feeding, as Dobell's solution or simple boric acid solution, will certainly lessen the risk of duct infections.

In abdominal operations where the patient is on rectal alimentation and consequently has not the regular stimulation of the salivary secretion, one should order, in addition to the mouth wash, the chewing of gum or wax, or better still the sucking of the old-fashioned lemon sugar stick which acts as a distinct stimulus to the salivary flow. Once the inflammation is established an application of either heat, in the form of a hot-water bottle, or cold, in the form of a light ice-bag, should be tried, and indeed sometimes suffices. Starr believes that while local application of the tincture of iodin or of a mercurial ointment is useful, it is not nearly as effective as an ointment of ichthyol (gr. xx) with lanolin (1 ounce). Before this is applied, the skin over the inflamed parotid should be washed with warm water, then carefully dried and the ointment gently rubbed in, some being left on the surface and covered with cotton wool or flannel and gutta-percha tissue. This dressing should be freshly made each morning and evening.

A surgeon, however, should watch the gland carefully and, in the event of fluctuation appearing, or even if the condition remains stationary for a period of five days, free incisions should be instituted. The incision should be made with the usual antiseptic technic and so directed as to avoid the larger blood-vessels, the facial nerve and Steno's duct, and should be packed with iodoform gauze and covered by an antiseptic dressing. The wound should be dressed daily until granulation has occurred. When the inflammation is followed by induration, potassium iodid should be given internally and a compressive bandage used locally. In these cases Starr recommends the additional use of some ointment as calomel (gr. x) and vaselin (1 ounce).

Chronic Inflammation.—This condition occurs following the prolonged use of mercury and potassium iodid, exposure to copper and lead salts and occasionally an attack of the acute epidemic parotitis or mumps. A form associated with duct infection as a result of sialodochitis fibrinosa, calculus and cicatricial stenosis is probably more frequent. Blumenthal

noted many cases of chronic parotitis in the German army during the last year of the War, due possibly to bad oral hygiene.

Treatment.—Treatment consists in: (1) removal of the exciting cause where such can be recognized; (2) careful and thorough oral antiseptics; and (3) local fomentation, either hot or cold, followed by massage; in some cases dilatation of the duct by filiform bougies is justified.

Sialodochitis Fibrinosa (*Whartonitis*).—It was first suggested by Kussmaul in 1879, and later confirmed by Emden and Greig that fibrinous or even purulent plugs might obstruct the salivary ducts, just as similar plugs are found in the bronchi of fibrinous bronchitis. These plugs result in an intermittent swelling of the salivary gland (especially the submaxillary) with an associated discomfort and even dysphagia for a few days, until it is terminated by the expulsion of the obstructive plug and the liberation of the accumulated saliva. The onset of symptoms is extremely sudden and there is a complete absence of constitutional symptoms.

The *treatment* is similar to that of chronic inflammation of the salivary gland.

SALIVARY CALCULI

As a result of bacterial infection in the duct in the presence of some foreign body as tartar, fruit seeds, etc., calculi may form either in the duct itself or in the gland acini. These stones are made up of organic matter, calcium phosphate and calcium carbonate with traces of iron, magnesium, etc. They are usually oval-shaped, if formed in the duct, but round or irregular if formed in the gland substance. They are generally single, but may be multiple.

Of some 300 cases collected by Erdman, 66 per cent occurred in the submaxillary gland or its duct, while only 20 per cent were found in the parotid or its duct, and but a few cases in the sublingual gland. The symptoms are salivary colic, which is particularly apt to occur during a meal, and swelling of the affected gland, most commonly the submaxillary. The attack generally terminates with a profuse discharge of saliva, but sooner or later an inflammation and possibly suppuration of the gland develops with the usual local and general manifestations. Diagnosis by the X-ray film is all too often negative because of the relation of the stone to the jaw bone. A careful history and palpation of the floor of the mouth are therefore more useful.

Treatment.—Apart from prophylaxis this is entirely surgical. Dilatation of the duct and gentle massage may permit of the extraction of the stone. In other cases incision along the course of the duct within the mouth is necessary. In chronic cases with a badly inflamed gland complete excision of the gland seems justifiable.

SALIVARY FISTULA

While salivary fistula was first described in the time of Galen, it is a very rare condition in civil practice. During wartime, but particularly during the recent World War, wounds of the face and jaw were not infrequently complicated by a salivary fistula. These are of two types: (1) fistulæ of the ducts; or (2) fistulæ of the gland proper. They are both equally distressing to the patient owing to the great inconvenience from the profuse salivary discharge that occurs more or less constantly with a great exacerbation at meal times, and secondly to the resultant disturbance of health from interference with proper digestion from the loss of the salivary secretion.

Treatment.—Many methods have been tried in the past with varying success; among others one must mention: (1) compression; (2) cauterization with silver nitrate or the thermocautery; (3) compression of the carotid and ablation of the parotid gland; (4) ligation of the duct; (5) obliteration of the duct by some foreign body as phenolated oil or salts of luminary; (6) the creation of an intrabuccal opening by transfixion; (7) removal of the auriculotemporal nerve or the injection of the nerve sheath with 3 c.c. of alcohol. Less radical measures, such as massage and the application of hot-air currents, have in some cases been successful and are worthy of trial as adjuvants at least. Radiation in the form of radium exposures or X-ray has also been successful. Cole and Knox recommend 200 mg. of radium in platinum tubes of about ½ mm. thickness applied to the region of the fistula; lead sheeting of 3 mm. thickness is employed to cut off the majority of the hard beta rays and yet permit of the radiation of the gamma rays. The radium is enclosed in rubber tubing and wrapped in several layers of lint to cut off any secondary radiation from the metal filters. An exposure of three to four hours to each skin area is recommended. When the X-rays are used in addition they are filtered through 2 mm. of aluminum. The best results reported are those of Pietri who claims to have cured 38 cases of salivary fistula by means of a fixation mask binding the jaws in a position of constant rest, enforcing absolute silence on the part of the patient and allowing only a liquid diet for a period of several weeks. By this means a prolonged rest is afforded to the salivary gland and eventually a granulation of the fistulous opening.

SPECIFIC INFECTIONS

Syphilis.—Syphilis in both the secondary and tertiary stages of the acquired form, and very rarely in the congenital form, may affect the

salivary glands; in fact whenever a painless bilateral enlargement of the parotid glands occurs one should always think of the possibility of syphilis. Occasionally there is an associated involvement of other groups of the salivary glands. The course may be acute or subacute, but is more usually chronic. The gland presents a firm consistency with an irregular surface, but usually no tenderness. It may form a tumor the size of a lemon. In the secondary stage other luetic stigmata are present, but in the tertiary stage even the Wassermann test may prove negative.

Treatment consists naturally in the use of antisyphilitic measures, particularly arsphenamin. Caution must be exercised in the administration of mercury as many feel that it may be one of the exciting factors in the production of the parotitis in the tertiary group. However, if proper care is taken of the mouth by means of the frequent use of a potassium chlorate mouth wash, it seems to the writer that there is little risk of using mercury in the usual dosage in such patients. Potassium iodid in the tertiary cases must also be used in full doses, but with frequent intermissions.

Tuberculosis.—This rare disease of the salivary glands merits only a passing reference. It probably results from a blood infection or the breaking down of a lymphatic gland inbedded in the substance of the parotid or submaxillary gland. Because of its slow development it may be mistaken for a mixed tumor.

Treatment is supportive and the free drainage or, better, the radical removal of the involved gland.

Actinomycosis.—Actinomycosis of the salivary glands has been reported by Johnson and more recently by Soederlund; the latter has seen 4 cases of this rare affection of the salivary glands. In all there was a diffuse inflammatory enlargement of the entire gland, but with a relatively painless course. He states that there are now 10 cases of submaxillary and 7 of parotid involvement anatomically confirmed.

Treatment should consist of moist heat externally and the internal administration of potassium iodid. In addition it may be possible to excise the small primary focus, but it is rarely if ever necessary to remove the entire gland.

LYMPHOMATA

(*Mikulicz Syndrome*)

While Mikulicz in his original description considered the bilateral symmetrical enlargement of the salivary and lacrimal glands as a distinct entity, we have described it as a syndrome because of its occasional association with such diseases of the lymphatic and hemapoietic systems as Hodgkin's disease, pseudoleukemia vera and lymphocytic leukemia. Occa-

sionally the syndrome is seen in patients with syphilis, though rarely in such cases is it of the fully developed type. In two fairly extensive reviews of the literature in 1909 and 1920 we were able to find some 95 or 100 cases, the majority of which were unassociated with changes in the lymphatic or blood-forming organs and were considered as Mikulicz disease proper. Even in this group one found incomplete cases and we concluded that many of the chronic unilateral or bilateral enlargements of the parotid, submaxillary, sublingual or even of the lacrimal glands were illustrations of the lymphomatous hyperplasia that is seen in the fully developed case of Mikulicz disease proper.

Space does not permit of further details about this interesting group of cases. Suffice it to say, that in some the secondary salivary glands of the hard palate, the Blandin-Nuhn on the under surface of the tongue and the Weber's glands of the posterior and lateral portion of the tongue may also be enlarged. The tumors so formed are firm, smooth, painless, free from tenderness, and are usually not adherent to the surrounding tissues. The function of the glands may or may not be deranged. More commonly there is xerostomia, rarely salivation and lacrimation.

Treatment.—Various drugs have been recommended internally, of which the most useful are no doubt arsenic in the form of Fowler's solution and potassium iodid. They may either be given in alternate courses or at the same time, though at separate hours of the day because of the chemical incompatibility of the two drugs. Massage, faradism and galvanism have been very disappointing. X-rays have been tried in a number of cases with apparent benefit; they must be used with caution and with the proper filtration. In some cases the removal of foci of infection as tonsils and adenoids has proved of assistance. For esthetic purposes extirpation of the tumors may be resorted to, but as a general rule surgical intervention is unnecessary unless there be a suspicion of lymphosarcoma.

In the more recent literature a suggestion has been made that there is a close relationship of the salivary glands to those of internal secretion (Mohr, Nagel, Dalché and Haemmerli). On this account a trial of the thyroid extract and possibly of the ovarian extract would seem justifiable in these chronic maladies.

TUMORS: BENIGN, MALIGNANT AND MIXED

Benign tumors, such as lipomata, adenomata, chondromata, hemangiomata, lymphangiomata, and malignant varieties, such as lymphosarcomata or pure sarcomata, occasionally occur. The most usual tumor is the mixed tumor of Billroth. The mixed tumors form probably 95 per cent of the tumors of the salivary glands. Boehme found that the

parotid gland was affected in 74 per cent; the submaxillary in 7.7 per cent and the sublingual in 1.1 per cent of the reported cases up to the year 1892. It is not the function of this article to discuss the great diversity of opinion as to the exact origin and consequently the proper classification of these tumors. By some they have been regarded as epitheliomata; by others as endotheliomata, and by still others as sarcomata. The majority are in accord with Wilson and Willis, who conclude that the mixed tumors of the parotid are mesotheliomata of embryonic origin. Pathologically, they vary considerably from fibrous tumors without mucoid or cartilage formation to very hard, dense tumors containing large amount of cartilage. There are some very soft cellular tumors with trabeculæ of transparent mucous tissue running into and surrounding the area of parenchyema. Still others closely resemble the carcinomata.

The tumor is, as a rule, first a small movable nodule in front of the ear, but soon fills up the retromandibular fossa. On account of its attachments to the fascia, the growth of the tumor is forward and downward into the neck. The symptoms consist of pain, dysphagia and salivation; while late in the course emaciation and cachexia may supervene.

Treatment.—Because of the possibility of these tumors developing a malignant character, early radical surgery is the only safe procedure and in skilled hands is unassociated with any serious risk. It must be confessed, however, that a complete removal of the parotid tumors is often impossible and that the portion left behind may take on a more rapid malignant growth; hence, it is always well to follow any radical surgical procedure by repeated applications of radium or X-ray therapy. Care of the general health is of course also indicated.

REFERENCES

Blumenthal, W. Verdickung der Speicheldruesen bei Kriegteilnehmern, Deutsche med. Wchnschr., xlv, 1141, 1142, 1919.

Boehme, H. Zur Kasuistik der Speicheldruesengeschwuelste, Diss., Berlin, 1892.

Cole, P. P., and Knox, R. Fistula of Parotid in War Wounds of Face and Jaws, with Note on Radiation Treatment, Lancet, i, 971, 972, 1919.

Dalché, P. Hyperparotidie, Presse méd., xxviii, 785, 786, 1920.

Erdman, S. Calculus in Salivary Ducts; Report of Five Cases, Journ. Am. Med. Ass., lxxiv, 1447-1450, 1920.

Haemmerli, A. Speicheldruesenhyperplasie und Erkrankung endrokriner Druesen, Deutsches Arch. f. klin. Med., cxxxiii, 111-124, 1920.

Howard, C. P. Mikulicz Disease and Allied Conditions, Internat. Clin., Series 19, i, 31-64, 1909.

Howard, C. P. Diseases of the Salivary Glands, Nelson's Loose-Leaf Medicine, v, 21-33, 1921.

Hutchinson, J. A Case of "Dry Mouth" (Aptyalism), Tr. Clin. Soc. London, xxi, 180-181, 1888.

Johnson, R. A Case of Actinomycosis in the Parotid Region, Ibid., xxxiv, 235, 1901.

Kraus, F. Klinische Pathologie der Sekretionsorgane, Nothnagel's Spec. Path. u. Therap., xvi, 77-103, 1902.

Mikulicz, J. Ueber eine eigenartige symmetrische Erkrankung der Thraenen und Mundspeicheldruesen, Beitr. z. Chir., 1892.

——— Festschrift z. Billroth, 610.

Nagel, J. Die Klinische Bedeutung doppelseitiger chronischen Speichel- und Traenendruesenschwellungen, Ztschr. f. klin. Med., lxxxiii, 358-380, 1916.

Pietri, P. Absolute Repose of Jaws as Treatment for Traumatic Parotid Salivary Fistulæ, Ann. Otol., Rhinol. and Laryngol., xxvii, 1333-1347, 1918.

Soderlund, G. Actinomycosis of Salivary Glands, Acta Chir. Scandinav. (Stockholm), liii, 189-229, 1921.

Starr, L. Diseases of the Salivary Glands, Forchheimer's Therapeusis of Internal Diseases, iii, 26-29, D. Appleton & Co., 1914.

Wilson, L. B., and Willis, B. C. The So-Called Mixed Tumors of the Salivary Gland, Am. Journ. Med. Sc., cxliii, 658-870, 1912.

CHAPTER XXVII

THE TREATMENT OF DENTAL DISEASES AND THEIR RELATION TO GENERAL HEALTH

KURT H. THOMA

The recognition of the effect of general diseases on the teeth and the tissues of the mouth and the relation of dental defects and infections of the jaws on other important organs of the body has brought about a much closer relation between medicine and dentistry. The dentist often needs to consult a physician or specialist in one of the medical branches and, on the other hand, because dental diseases play a great rôle in many conditions met in internal medicine, orthopedics, pedriatrics, rhinology, otology, ophthalmology, neurology and preventive medicine, the physician needs to understand the pathology of dental lesions, their treatment and the dentist's point of view. Only through such understanding does intelligent coöperation become possible, an understanding which is necessary for the welfare of the patient. Dentistry has made great strides the last few years. Half a dozen subspecialties have been developed. Originally a mechanical art, it has been adjusted to its proper relation to medicine. The writer will attempt to give the general practitioner of medicine an up-to-date idea of the principles of treatment of the diseases of the mouth and the teeth which will enable him to give advice to his patient when the need arises. It should be borne in mind, however, that dental treatment involves many intricate technical problems, which, though unimportant from a general point of view, often mean a great deal as far as the comfort, masticating ability and health of the patient is concerned. For a final opinion no one but an expert should be consulted, one who makes a specialty of diagnosing dental diseases, who is able to make a painstaking clinical and roentgenological examination and who is not only familiar with oral pathology, but also well trained in the various technical problems of dentistry. He should be a consultant who understands the physician's problem but still keeps in mind the dental aspects.

THE DEVELOPMENT AND CALCIFICATION OF THE TEETH

Hard and well-formed teeth resist decay while poor and defective teeth easily fall prey to the attacks of disease. The quality and hardness of the tooth depends upon the process of calcification, especially during the time when the enamel, which is the only part of the tooth exposed to outside influences, is formed. This takes place in deciduous teeth from the nineteenth week before birth to the sixth month after birth. The quality of the first set of teeth depends mainly upon the mother's supplying during pregnancy and the nursing period the material necessary for strong teeth.

No permanent teeth begin to calcify until after the child is one year old, with the exception of the first permanent molar, whose cusps are

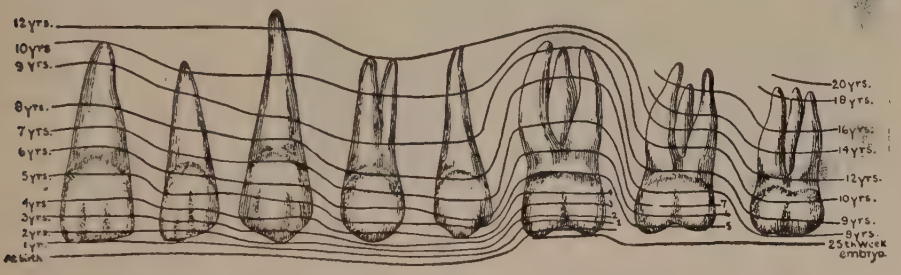

Fig. 1.—Progress of Calcification of the Permanent Teeth.

calcified at birth. The time when calcification of the crowns is completed varies greatly with the different teeth (see Fig. 1). At the age of nine all are finished except that of the third molar. Any influence which might benefit the calcification of the permanent teeth must therefore be exerted between the time the child is weaned and the age of twelve.

The Effect of Acute Infectious Diseases on the Teeth.—In the exanthematous fevers we find that changes occur on the mucous membranes of the mouth which are so characteristic that they are even pathognomonic. When sufficiently acute they also cause disturbances in the calcification of the developing teeth. This is especially true of measles and scarlet fever, with their well-known effects on ectodermal structures, especially when occurring between the ages of one and four. The defects appear as pits and fissures or grooves more or less pigmented a brown or yellow color. Their location varies on the different teeth, following the lines of calcification, indicating the amount of tooth development that has already taken place at the time when the disease occurred (Fig. 1). The defects, therefore, appear principally on the enamel of the permanent incisors, cuspid and first molar (Fig. 2). The immediate cause has not

yet been absolutely determined. While some investigators are of the belief that the enamel defects spoken of as hypoplasia are caused by a detrimental action on the enamel-forming ameloblasts, by the bacteria or their toxins, there are others who claim that they are produced by a disturbance of the process of calcification during the time of the disease.

Therapeutic Measures.—Besides the routine treatment, the patient should be placed on a diet which has an abundance of the elements necessary for bone formation. To prevent secondary diseases in the mouth, such as stomatitis and bone necrosis, which are especially liable to appear during or after the measles or scarlet fever, careful prophylactic treatment of the mouth is necessary. It has been observed that children with badly decayed teeth are liable to be more seriously ill and more prone to relapse. The mouth should be washed several times a day with hydrogen peroxid, which can also be used as a gargle or a spray. If lesions have already formed, the use of the following powder can be recommended, 3 parts of Flor. sulphur. and 1 part of sodium sozoiodolici, to be applied with a powder blower. After the termination of the disease the teeth often fall prey in a surprisingly rapid manner to the ravages of decay for which reason a visit to the dentist should be recommended, even though the child has but the first set of teeth.

FIG. 2.—HYPOPLASIA CAUSED BY SOME GENERAL DISEASE AFFECTING THE TOOTH FORMATION AT THE AGE OF THREE. Note the pits and grooves on teeth A, B, and C.

Rachitis from the Dental Point of View.—In rickets the upper jaw is often V-shaped, very pointed in front and with a high and narrow palate. The lower jaw shows the effect of the geniohyoid and geniohyoglossus muscles drawing back the entire incisor region, the teeth standing either in a straight line from cuspid to cuspid, or even receding behind this line. The teeth may be changed in size as well as in form and often a hypoplasia or malformation of the enamel and certain changes in the dentine occur.

Treatment.—To correct as much as possible the structural changes in the temporary teeth of the rachitic child and prevent them in the

permanent teeth one should give the children a diet that favors calcium metabolism. If there are no contra-indications this should be started at as early an age as possible. Even in older rachitic children, when the teeth are formed, an improvement can be effected because calcium metabolism continually takes place in the vital tooth so that the tooth tissue becomes more resistant to decay.

Congenital Syphilis.—The teeth in inherited lues often erupt very much later than normal. More important, however, are the defects in the enamel. These defects are produced by pathological conditions affecting the enamel-forming cells of the tooth germ in which lesions containing Treponema pallidum have been demonstrated. The upper central incisors, of the permanent teeth,[1] are most frequently affected, showing on the cutting edges crescent-shaped notches with brownish discoloration. Their sides are convex with the angles rounded off. These peg-shaped teeth with the half moon defect are known as hutchinsonian teeth. The first molars are often entirely flat, because the cusps have failed to develop and more rarely they are almost denuded of enamel. In the permanent set the condition is more frequent, because the influence of the syphilitic lesions seem to be most active at the time of calcification of the cutting edge of the permanent central incisors and the cusps of the first permanent molar, that is, the last two months of fetal life and the first year after birth, but the central incisors of the deciduous set have also been found affected.

THE ERUPTION OF THE TEETH

Occasionally we find babies born with two or more front teeth. These may belong to the deciduous set or are in rarer cases special formations. If the latter is the case, they are generally loosely attached and fall out very shortly to be replaced by those of the deciduous set. The early eruption of the first teeth, especially the incisors, is more frequent. This is of no serious consequence as it does not generally interfere with nursing. The time when the deciduous and permanent teeth normally erupt is given in the table on the following page.

Difficult Eruption of the First Teeth.—When a tooth is ready to erupt, the part of the gum immediately over the erupting tooth appears white. A certain amount of pain may be caused by pressure against the gum but generally disturbances from the eruption of a tooth are caused after it has broken through. This is especially the case in molars. Pockets form between the erupting crown and the gum in which food remnants may lodge, starting an irritation. The gum lying over the partly

[1] Current medical teaching holds that only the permanent teeth show the hutchinsonian deformity.—Editor.

CHRONOLOGY OF HUMAN DENTITION

	Tooth	Time Calcification Begins	Time Calcification Is Completed	Time of Eruption	Time Tooth Shed
Temporary Teeth	Central incisor	4th fetal month	17th to 18th postnatal month	6th to 8th postnatal month	7th year
	Lateral incisor	4th fetal month	14th to 16th postnatal month	1st to 9th postnatal month	8th year
	Cuspids	5th fetal month	24th postnatal month	17th to 18th postnatal month	12th year
	1st molars	5th fetal month	18th to 20th postnatal month	14th to 15th postnatal month	10th year
	2d molars	5th to 6th fetal month	20th to 22d postnatal month	18th to 24th postnatal month	11th to 12th year
Permanent Teeth	Central incisor	1st year	10th to 11th year	7th to 8th year	
	Lateral incisor	1st year	10th to 11th year	7th to 8th year	
	Cuspids	3d year	12th to 13th year	12th to 13th year	
	1st bicuspid	4th year	11th to 12th year	10th to 11th year	
	2d bicuspid	5th year	11th to 12th year	11th to 12th year	
	1st molar	8th fetal month	9th to 16th year	6th to 7th year	
	2d molar	5th year	17th to 18th year	12th to 14th year	
	3d molar	9th year	18th to 20th year	17th to 20th year	

The lower teeth generally precede those in the upper jaw by short intervals.

erupted tooth often becomes infected, leading to a gingivitis and in very rare cases to abscess formation. The inflamed gum may cause discomfort in the act of nursing.

It seems to be a firmly established belief among the laity that a child must be more or less ill when cutting a tooth and at one time or another teething has been connected with most diseases occurring in infants, such as eczema, urticaria, tooth cough, tooth cramps, diarrhea and other digestive disturbances. This often leads to regrettable neglect of the first symptoms of illness, even among the best-intentioned mothers. The writer believes that beyond local discomfort, which perhaps may cause general nervousness, irritability and restlessness, there are no severe general symptoms connected with the eruption of the teeth.

Therapeutic Measures.—Lancing of the gums is only indicated in case of severe pain and in case of partly erupted teeth. Where the gum is inflamed or infected it is even contra-indicated. One should apply boric acid solution or other mild antiseptics. Rubbing the gum with a sterile piece of rough cloth, using the tooth as a cutting edge, is better than cutting and generally gives a great deal of relief.

As a preventive measure the parents should be advised to give the babies during this period stale hard bread crusts on which to bite, thus facilitating dentition.

ABNORMAL DEVELOPMENT OF FACE AND MALOCCLUSION

"Dentofacial maldevelopments," writes Dr. Alfred Rogers, "are prevalent in children of all civilized races. These defects do not seem to be confined to any class, the children of the rich and middle classes suffering as well as those of the poor. Many children, who are apparently in a state of general bodily health and vigor, are found to be sufferers from dentofacial maldevelopments in varying degrees. It may be said, however, that the severer cases, those which may be regarded as actual deformities, are more apt to be found among children whose life histories show arrested development, following periods of lowered vitality. These maldevelopments may be confined to the teeth and the dental arches, or they may, as in severer cases, involve the contiguous bony structure of the maxilla and mandible and the soft tissue of the face.

"Heredity as an etiological factor in malocclusion is not yet clearly understood. Some investigators think that any feature which resembles the parent or grandparent is inherited, whereas it may be due to a like environment. Yet there are some very clearly defined developments of the jaws and teeth which are, no doubt, germinal in their character, and are, therefore, inherited."

It is sometimes thought that malnutrition has much to do with the malformation of the osseous tissue which forms the framework of the teeth, but investigations in this direction are not yet conclusive enough for final judgment as to the extent of its influence.

Habits forced upon the child tend to influence the development of his entire body. Habits of eating in most civilized countries, and especially America, are such as to limit the functional activity of the masticatory apparatus. To determine how important a rôle mastication plays in the growth of the face and jaws, Baker made the following experiments. He selected young animals and extracted or ground the teeth short on one side so that mastication was possible only on the other. The result was very remarkable. There was a decided difference in the development of the two sides of the jaws. The side where the teeth were not mutilated and where mastication was normal developed much more than the unused side. Not only were the jaws affected, but the entire head, including the cheek-bone and nose, presented a unilateral development, the whole face being twisted to one side.

There are other etiological factors of a mechanical nature such as too early loss or too long a retention of the deciduous teeth. There are certain pernicious habits such as thumb, finger, lip and tongue sucking. Narrow jaws and face are frequently due to mouth breathing, caused by constricted nasal passages which overthrows the muscular balance of

the face. Such cases are generally associated with adenoids, a vicious circle exists and these conditions must be treated.

Treatment.—The physician who takes care of the child has the first opportunity to observe the early symptoms of malocclusion. In many cases his coöperation is necessary to make possible orthodontic treatment by building up an undernourished child. The dental treatment consists of restoring normal occlusion, and Dr. Rogers writes, with modern scientific methods the orthodontist is able to undertake the treatment with very little discomfort to the child. Seldom should a child be conscious of discomfort in masticating its customary food for more than a few hours after the adjustment of the mechanical apparatus and frequent visits covering a long period of time are not necessary. In addition he advises to give the young patients a well-balanced system of exercises for the various groups of facial muscles in order to restore them to normal and to cure the habit of mouth breathing.

IRREGULAR ERUPTION OF TEETH

Retention of Deciduous Teeth, Due to Absence or Impaction of Permanent Ones.—In certain conditions the deciduous teeth remain and are not replaced by permanent ones. This happens when the permanent teeth are congenitally absent and also in cases in which the permanent teeth are prevented from eruption on account of impaction or misplacement. While we occasionally find that such deciduous teeth remain for a long time without becoming loose, we more often see in the Roentgen picture that the absorption of the roots proceeds as usual whether the permanent tooth is impacted or missing.

Congenital Absence of Deciduous and Permanent Teeth.—There are many cases in which a permanent tooth may be congenitally absent and usually there is a history that there were no deciduous ones either. This is considered by many writers as a forerunner of reduction in the human dentition. It is especially the third molars and the lateral incisors which are found to be missing.

Supernumerary Teeth.—It is believed that supernumerary teeth are a retrogession, or falling back upon the formula of a lower type, but there are also so-called rudimentary peg-shaped teeth which appear occasionally in the dental arch. These are caused by epithelial remnants, parts of the tooth band forming a primitive enamel organ into which a connective tissue papilla grows, so forming, by an analogous process as in tooth development, more or less well-formed supernumerary teeth.

Misplaced Teeth.—Unerupted teeth may be found in any part of the maxilla or mandible and it is important to include in the Roentgen

diagnosis such places as may harbor them; namely, the nasal cavity, the maxillary sinuses, the lower border of the mandible and the entire ramus.

Unerupted and Impacted Teeth.—Unerupted and impacted teeth may be found in various positions and, although often lying dormant for years, they may at any time become associated with neuralgia or dull pains in any part of the head or neck. Their efforts to grow to the surface are usually intermittent, which accounts for the fact that the symptoms are not constant. The pressure which they frequently bring to bear upon the tissues toward which they are growing causes at times a physiopathological absorption, for example, the distal surface of the second molar

Fig. 3.—Unerupted Upper Third Molar, Impacted against the Roots of the Second Molar.

root may become absorbed from the pressure of the cusp of an unerupted third molar. Judging by careful study the writer believes pain is not necessarily due to pressure against the obstruction part, but may be caused by development of the roots of an incompletely formed tooth in the opposite direction, when the inferior alveolar nerve is encroached upon. Such a case is shown in Figures 3 and 4.

The cause of these conditions is underdevelopment of the jaws, on account of which there is not room enough for all the teeth. The third molars, being the last to erupt, are principally affected. The irregularities generally causing impaction of the other teeth are premature loss or abnormal retention of the deciduous teeth. The cuspids are quite frequently impacted and unerupted, but any tooth, deciduous as well as permanent, may become an offender.

Infectious processes are often associated with impacted teeth and may

start from a blind abscess on a neighboring tooth or from a pocket on the gum.

Partly erupted teeth are more liable to become infected than entirely unerupted ones on account of the entrance of the fluid of the mouth into the opening made by the erupting cusp. The infection passes rapidly into the deeper tissues, because the soft tissue does not adhere to the enamel of the crown, and leaves a pocket, which offers a splendid chance for infection. The process of inflammation sometimes takes a chronic course with intermittent, subacute attacks, or it may be acute from the start. It then involves the surrounding tissues and if it is in

Fig. 4.—Unerupted Third Molar in the Mandible (Horizontal Position) Causing Absorption of the Distal Root of the Second Molar.

the back of the mouth may cause inflammation of the fauces and muscles about the ramus. Pharyngitis and trismus of the muscles of mastication are commonly sequels to an infection around a lower impacted third molar. Roentgen diagnosis is not only very useful in determining whether a missing tooth is unerupted and impacted, but is also an aid in studying the relation of such a tooth to the surrounding parts, in order to decide on the operation which is required. The roentgenogram should, therefore, show the entire outline of the tooth, and include a fair amount of the surrounding bone tissues.

Treatment.—The treatment is surgical. Entirely unerupted teeth which cause no symptoms may remain quiescent for an indefinite time; partly erupted teeth should be removed by operation at as early a time as convenient on account of the danger of infection. The best treatment of infection associated with an unerupted or infected tooth is prompt removal and subsequent antiseptic irrigation.

THE SALIVA

The function of the saliva is first that of a solvent: dry and solid food is softened, becoming saturated entirely during the process of mastication. It produces a medium which is important for mouth digestion of carbohydrates, which takes place through the action of the ferment known as ptyalin, and it finally lubricates the food bolus to facilitate its passage along the esophagus. Thorough mastication is necessary not only for the mechanical preparation of the food, but to induce an abundant flow of the saliva through the action of the muscles on the salivary glands.

Among the normal constituents of saliva are included mucin, albumin, ptyalin; also oxidizing enzymes, ammonium salts, nitrates, potassium sulphocyanate, alkaline phosphates, and chlorids, with traces of carbonates; urea, creatinin and in fact practically all normal constituents of the blood; and, in the sediment, epithelium cells, occasional leukocytes, and fat globules.

The abnormal constituents include glycogen, dextrin, rarely sugar, cholesterin, derivatives from bile, lecithin, xanthin bodies or alkaline urates, acetone, lactic acid, and crystalline elements resulting from insufficient oxidation or perverted glandular function.

H. Carlton Smith of the Department of Chemistry in Harvard University Dental School has done considerable work comparing some of the salivary constituents with those of the blood and found a significant similarity between the two analyses. He writes that his experiments show a very direct relationship which may frequently prove of value in detecting pathological conditions. The substances in the saliva which in our experience seem to follow the same curve as in the blood are urea nitrogen, creatinin, and uric acid. The urea nitrogen and creatinin seem to increase invariably in cases of nephritis corresponding to the rise of those substances in the blood, although the actual quantities found are always less. The uric acid content of saliva is a subject of very recent investigation but it seems now at least to be one of the most valuable from a diagnostic point of view. In every case of apical infection or pus absorption from teeth or maxillary sinuses which has come recently under the author's observation (about 50 cases), the uric acid content of the saliva has been double or more than double that in people with perfectly healthy mouths. The determination is so simple and results so far have been so invariable that it would certainly seem to be one of the most promising new suggestions in regard to salivary analysis and of great value in detecting pathological systemic conditions. The direct relationship between high uric acid in the blood, as well as in the saliva, and pus absorption is unquestionable.

PYORRHEA ALVEOLARIS

Pyorrhea alveolaris, Riggs' disease, or pericementoclasia as it is called now, is a disease of civilization, affecting man as well as his domesticated animals. This disease became very rampant among the Romans after the army returned from Asia Minor introducing new methods of cooking. During the two centuries that followed, the diet became very elaborate, sumptuous feasts were of everyday occurrence and a profusion of delicacies were served. Celsus, the celebrated physician of that time, made the statement, "The sad workings of a superior civilization is the cause of the decadence of our health." To-day pyorrhea is one of the commonest diseases in this country.

Gingivitis.—The etiology of the disease has been a matter of dispute for many years and a specific cause has been searched for eagerly but without result. The best opinion to-day is that it is a symptom complex in which a variety of constitutional as well as local causes are concerned. The writer believes that there are always certain predisposing causes, which not only lower the resistance of the gums, allowing the local conditions to become effective, but which also contribute to the chronicity of pyorrhea. A gingivitis always precedes pyorrhea and is caused by digestive disturbances, faulty metabolism, improper elimination and intestinal auto-intoxication. The patient is liable to show a considerable salivary acidity, together with high urinary acidity. Usually increased indoxyl, high ammonia and frequently high uric acid are found in both saliva and urine. Such an analysis is an indication of insufficient oxidation caused by overeating, poor elimination and lack of exercise. Glycosuria (not related to diabetes), also an indication of low oxidation, is, according to Smith, more or less associated with pyorrhea. Examination of pyorrhea patients from the Harvard Dental School Clinic showed that 25 per cent had alimentary or renal glycosuria. Inflammation of the gums is also often seen in diabetes (gingivitis diabetica) when the gums show a swollen spongy appearance with a dark red margin. Bleeding and pain are other symptoms and the tongue has a changed appearance; it is swollen and thickly coated and shows on the side impressions of the teeth. Another type of gingivitis is found during pregnancy (gingivitis gravidarum), beginning generally after the fourth month, and expresses itself as a hyperemia of the gum margins with tendency to hemorrhage from trivial causes. Gingivitis dysmenorrhoica is similar except that the margin of the gums remains normal but the remainder is red and hyperemic. Other predisposing diseases are nephritis and gouty or tubercular diathesis. The recent work of McCollum, Howe and Grieves shows that so-called deficient diet, especially that which produces scurvy, causes in animals pyorrhealike lesions. On account of disease of the gums being

a well-known scorbutic symptom in man, it is still a question whether or not the lack of the antiscorbutic or vitamin C in the diet may under certain circumstances cause pyorrhea without producing scurvy.

Local causes aggravate the condition, so that the disease progresses very much faster in one place than in another. Figure 5 shows this particularly well. On the teeth marked A, B, and C, the destruction of the bone has progressed almost to the apex of the root of the tooth. These local causes are unhygienic conditions, as soft deposits of food of a gelatinous or adhesive quality, such as are caused by white bread and cake which stick to the margin of the gum, then hard concretions on the teeth and food packed into the interdental spaces on places where the teeth are not in proper contact. Mechanical irritation caused by faulty crowns and bridges, projecting fillings and injury by toothpicks or the injudicious use of the toothbrush are other local etiological factors. A great deal of importance is laid on the even position of the teeth by most operators so that single teeth are not subjected to undue strain during mastication.

FIG. 5.—DRY SKULL SHOWING PYORRHEAL AFFECTION. Note the destruction of the alveolar process on various teeth.

The discharge of pus from the pyorrhea pockets is a constant danger to the patient's health. The infection may spread from the gums to the tonsils, and, by inhalation of moisture, globules laden with bacteria cause laryngitis, bronchitis, and catarrh. The swallowing of quantities of pus, mixed with food, results in digestive disorders. Hunter, who first called attention to the harmful effects of "oral sepsis," lays stress on the fact that pus from the teeth, when taken into the body with the food, is a cause of ulcers and other diseases of the stomach and intestines and also of severe anemia.

Pyorrhea alveolaris affects the gums and the teeth as well as the supporting bone. Its recognition in its early stages is of the greatest importance. The mouth of every patient should be watched for signs of gingivitis characterized by swelling of the small papillæ between the teeth. Later the gums become purple in color and bleed when the teeth are brushed or from the use of dental floss. This condition may last for a considerable length of time. The underlying tissues are next infected and

involve the attachments of the periodontal membrane around the neck of the tooth. The disease follows this membrane in preference to other tissue, penetrating deeper toward the apex of the tooth. The suppurative process causes disintegration around the bone of the tooth with the formation of so-called pus pockets. When this condition is once firmly established it is difficult to cure. The cementum of the tooth barred from its nutrient membrane becomes pus soaked and calcareous deposits form from the serum of the blood. These secondary conditions contribute to the chronicity of the disease. Abscess formation may occur between the roots of multirooted teeth and when the infection reaches the apex of the tooth it may involve the pulp.

Treatment.—The systemic faults should be eliminated because the treatment of the dental condition is not very satisfactory as long as general disease exists. In gingivitis due to pregnancy and dysmenorrhea careful hygiene of the mouth is of great importance. The application of tincture of myrrh can be recommended and great care should be taken that the condition does not develop into pyorrhea. Modification of the diet and improved habits of living (exercises and elimination) must be insisted upon if a systemic acidosis exists. Careful study of the dental causes and Roentgen examination to determine the extent of the disease will indicate the local treatment. All teeth which show evidence of apical infection or which have lost a great deal of support on account of extensive pockets should be extracted. The mouth must then be put in a perfect hygienic condition, removing all dental defects and establishing normal occlusion. Treatment of the remaining teeth can then be undertaken, and the help of the patient must be insisted upon in following carefully the instructions given for the home care of the teeth and gums. Regular prophylactic treatment by the dentist or oral hygienist is necessary for all patients with pyorrhea tendency at an interval of two or three months, according to the patient's ability to keep his teeth scrupulously clean. Early treatment is the secret of complete success; physicians and dentists, therefore, should give serious consideration to even a slight inflammation of the gums.

DENTAL CARIES

Dental caries is one of the most common diseases of the human race. From 85 to 95 per cent of the civilized people suffer from it and its consequences, infection of the dental pulp and alveolar abscesses. While the pathology and treatment of this disease is purely a dental problem, it is the physician, and especially the pediatrist, who can do more for its prevention, by regulating the diet of the expectant mother and the child so as to insure the formation of good bones and solid teeth. McCollum, whose work has already been referred to, stated in a paper recently read

before the Massachusetts State Dental Society that his latest researches disclosed that it was not the vitamin A but a fourth vitamin which had to do with calcification. The reason why this action was formerly attributed to the fat-soluble vitamin A is that it is practically contained in the same foods as the latter but not in the same proportion. It is abundant in cod-liver oil, less abundant in butter fats and to a far less degree in cocoanut oil. Vitamin A is absent in the last. His experiments prove that calcium salts cannot be utilized for the formation of teeth and bone unless the fourth vitamin is supplied in sufficient quantity.

When the mixed diet begins is the time when the calcium deficiency is apt to occur and the child's diet should be carefully watched with that in view. Unfortunately white bread, meat and sugar, the most popular foods, are deficient in calcium salts. In other foods the mineral salts are removed by peeling, while prolonged cooking removes them from the vegetables and the water which then contains the salt is usually thrown away instead of being used for soup. It is generally believed that inorganic calcium salts are not utilized but it has been found in practice that the drinking of limewater is effective. McCollum also says that precipitated chalk, a teaspoonful given every day, is an excellent way of supplying the needed calcium especially if given with cod-liver oil. Smith calls attention to the fact that there is no better way of administering calcium as well as all the other salts and vitamins than by fresh milk rich in mineral salts and butter fat. Other foods rich in calcium salts are milk, egg yolk, oatmeal, whole wheat bread, Irish and sweet potato, beans, cauliflower, celery, spinach, turnips, parsnips, olives and oranges. Sherman and Hawley state that "children do not seem to utilize the calcium of vegetables as efficiently as they do that of milk."

Every growing child should have at least a quart of fresh milk per day for proper development of its skeletal structure. Something should also be said here about dietary faults such as the use of an excessive amount of refined sugar or other sweets. Parents often believe that sugar is needed for the development and nourishment of the body and do not realize that the so-called craving for sugar is, in fact, a desire to indulge in the pleasure of its flavor, which leads to the formation of a habit which is very difficult to break. Sweetmeats not only spoil the appetite for normal healthy food but furnish ideal pabulum for the bacterial colonies called plaques, which adhere to the surfaces of the teeth and produce decay. The worst time to eat sweets is between meals and the abominable practice of some parents of giving their children candy as a bribe to induce them to go to sleep is an ideal method of producing dental caries.

Prophylaxis.—To insure development of strong well-calcified teeth and to prevent them from becoming decalcified the diet should contain the necessary amount of mineral salts and vitamins. It has been recommended to give the mother during the period of pregnancy and lactation inorganic

mineral salts with or without cod-liver oil. McCollum recommends a teaspoonful of precipitated chalk daily. Others recommend limewater. Uncooked milk, however, not only supplies all the vitamins but seems the best means of supplying mineral salts.

PULP AND PERIAPICAL INFECTION

Neglected or deep decay in a tooth causes infection of the dental pulp. This is generally associated with pain, first to cold, later to hot things taken into the mouth. Under certain conditions, however, the infection runs a chronic course and then no pain is experienced by the patient. In the first instance we get acute pulpitis with abscess formation while in the latter pulp necrosis is the result. A certain amount of absorption may take place from an infected pulp and if treatment is not undertaken in time the periapical tissues are affected. The writer believes that at first this represents but a protective reaction in response to the infection in the pulp, an accumulation of leukocytes or lymphocytes in the periodontal membrane, which increases in size.

Periodontitis.—In acute infection this inflammation of the periodontal membrane causes the tooth to be pushed out of the socket; every time the patient closes the mouth, the infected tooth necessarily comes first in contact and causes pain. In chronic infection of the pulp, the reaction is so slow that the increase in the size of the membrane is compensated by absorption of bone. This loss of bone can be demonstrated in a Roentgen picture.

Acute Periapical Infection.—This condition starts as acute periodontitis and involves a violent inflammatory reaction of the tissue. Purulent exudations soon accumulate, the cells of the peridontal membrane and the surrounding bone become destroyed and the condition is then called acute alveolar abscess. This may spread and cause suppurating ostitis of great extent, or the pus may soon find an outlet through the outer cortical layer via the haversian canals to the surface of the bone. When the pus collects under the periosteum, a reaction sets in at once, causing a widespread serous infiltration of the soft parts, cheek or neck. Finally the pus burrows a channel through the soft tissue, forming a fistula into the mouth, nose, maxillary sinus, or outside of the face. After this process of destruction has reached its climax, nature makes an attempt at repair and the acute symptoms disappear, but unless the cause (a diseased pulp or necrosed root apex) is removed the condition becomes chronic. In this stage it may last for an indefinite period with the fistula discharging pus if the destructive process becomes more active, or closing up for a time if the defensive system predominates, only to reopen with more or less marked subacute symptoms when suppuration again becomes more active.

Proliferating Periodontitis, Blind Abscess or Dental Granuloma.—This is a reaction to a mild infection from the root canal, such as occurs from a chronic periodontitis, incomplete or unsuccessful treatment of the root canal after removal of the pulp. A stimulation takes place forming inflammatory granulation tissue instead of breaking down the tissue by suppuration. An exacerbation, however, may change the pathological picture so as to simulate a typical acute alveolar abscess. The blind abscess, or granuloma, begins and continues to grow without giving any symptoms. The defensive system of the body takes care of the slight amount of pus formed, which is absorbed through the lymphatics, or blood channels. Histologically the lesion presents a picture of chronic inflammation with a predominance of lymphocytes forming into plasma cells; the blood picture is that of mild lymphocytosis. Figure 6 shows a photomicrograph of a bicuspid tooth with a granuloma attached. Note the vascular fibrous sac surrounding the lesion and protecting the neighboring tissue. In the center of the abscess are three places where the tissue is broken down into pus.

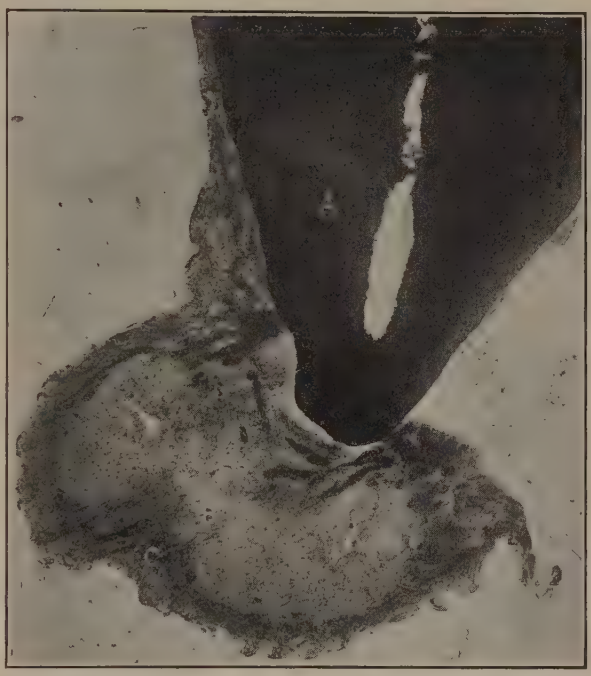

Fig. 6.—Photomicrograph of a Granuloma Stained with Mallory's Phosphotungstic-acid-hematoxylin Method to Bring Out the Fibrous Part of the Tissue. Note the strong fibrous capsule. The inner part of the granuloma shows centers where necrosis has taken place.

This pus continually formed in small quantities has generally no outlet, the original opening through the root canal and cavity in the crown having been closed by the filling. The pus is taken up by the blood-stream or lymphatics and carried away. If more pus is formed than can be taken care of and eliminated by means of absorption, it may result in the formation of a fistula. This is generally known as a gum-boil. Every one knows that a great deal of pus can be squeezed from a gum-boil several times a

day and this makes it easier to understand that such pus, when drained into the system, must be injurious to the health.

The condition of the root apex is of great importance. Periapical infection of long-standing causes changes in the cementum of the tooth. Nutrition is usually disturbed, the cells of the apical part of the periodontal membrane may become destroyed and the cementum, which is very porous and easily absorbs the products of inflammation, becomes pus-soaked and filled with bacteria. In this condition the tooth is an obnoxious foreign body which Nature tries to eliminate by osteoclastic absorption, starting on the surface of the cement, which then presents a roughened appearance. Marked indentations are formed and the cement, and later the dentin also, dissolves (Figs. 7 and 8). At times new cement is deposited, due to stimulation of cementoblasts, which have survived. This causes enlargements of the root end and often renders extraction of the tooth extremely difficult. The reason why an abscess of long standing is so stubborn and impossible to eliminate by any means other than surgical treatment is on account of the infection of the apical part of the tooth root, which is a dead piece of bone and, like a sequestrum, has to be removed before healing can take place. The condition of the bone around the root end is evidenced by progressive absorption, first of the dense part of the bone, the stratum durum lining the alveolar socket, and later of the trabeculæ of bone of the inner cancellous part of the maxillæ. By this process of rarefaction a definite cavity is formed which is filled in by the proliferating fibrous tissue of

FIG. 7.—PHOTOMICROGRAPH OF A ROOT TIP WITH GRANULOMA STAINED WITH MALLORY'S PHOSPHOTUNGSTIC-ACID-HEMATOXYLIN METHOD. Note the absorption of cementum (A) and the rough appearance of the surface of the dentin.

the granuloma just described. The disease causes a slow and gradual destruction of bone and at no time are any visible bone particles given off. It usually involves only a limited area but sometimes it is very extensive. Frequently the outer or inner cortical layer of the bone becomes involved and destroyed so that an opening is formed, covered by the periosteum and the gum (see Fig. 9). This causes a tenderness when applying pressure in a digital examination.

Fig. 8.—Photomicrograph of a Root End with Granuloma Showing a Great Deal of Absorption of Both Cementum and Dentin.

Roentgen Evidence.—The Roentgen picture shows the effect of the infection on the bone surrounding the apex of the tooth and on the tooth root itself. The bone destruction shows in the Roentgen negative as a dark area, which is a picture of the radiolucent bone cavity. We may generally take the size of an abscessed area as an indication of the seriousness of the involvement of the surrounding tissues. There is an exception to be made, however, in the bicuspid and molar regions of the upper jaw, especially if these teeth protrude into the maxillary sinus. It should be borne in mind that when there is only a very thin film of bone over the roots of such teeth there is no chance for extensive bone destruction, and cases which show the smallest shadow are more liable to be the cause of sinus disease than larger areas separated from the antra.

If the outer or inner cortical plate of bone has become perforated (Fig. 10) we get a deeper shadow than from a cavity in the cancellous bone between the two thick, unaffected cortical plates (Fig. 11). Again, if the apex of the root is close to the surface, as is often the case with upper

FIG. 9.—DRY SKULL SHOWING AN ABSCESS CAVITY IN THE BONE AROUND THE ROOT OF AN UPPER BICUSPID. Outer wall of the bone is destroyed. The root end of the tooth looks dark and necrotic.

incisors, we may find that there is only a shallow depression in the surface of the bone (Fig. 12) giving no Roentgen changes at all. Important information which the Roentgen picture gives in cases of periapical infection is the condition of the tooth tissues at the apex of the root. If the outline is indistinct or if actual loss of tooth structure is recognizable, we know

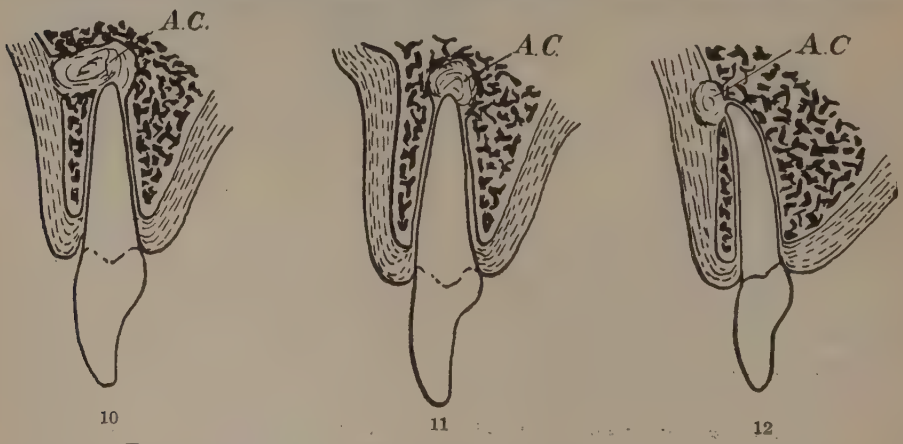

FIG. 10.—BUCCAL ALVEOLAR PLATE PERFORATED BY ABSCESS.

FIG. 11.—APICAL ABSCESS IN CANCELLOUS PART, CORTICAL LAYERS UNDISTURBED.

FIG. 12.—APEX OF ROOT NEAR SURFACE. The abscess tissue, formed under the periosteum, has caused only a shallow depression; cancellous bone undisturbed.

that the tooth apex is necrotic. The process of absorption indicates plainly that Nature wants this tooth removed.

Treatment.—If the dental pulp is diseased, it must be removed, and the most careful treatment is necessary to prevent future periapical infection. The condition of the periapical tissue must always be investigated. Acute periapical infection, as well as blind abscess or granuloma of short standing, is amenable to conservative treatment, especially in younger patients. Retention of a tooth would seem advisable if the Roentgen indications are favorable to root canal work.

In patients suffering from some chronic disease, or whose resistance is lowered, radical treatment is generally indicated. It is perfectly justifiable to be radical in such cases, not only with diseased, but even with suspicious teeth, because there is very little chance that under such conditions they can remain normal for any length of time.

Whenever apical necrosis and absorption are discovered in the Roentgen picture, indicating clearly that nature wants to eliminate an obnoxious foreign body, extraction is indicated, from a purely dental point of view.

MORE EXTENSIVE LESIONS CAUSED BY PERIAPICAL INFECTION

If we consider the frequency of dental infections it is surprising how rarely we find extensive bone infection and serious involvement of the adjoining structures and the alveolar process. The reason for this is probably to be found in the bountiful blood supply of the bone in the immediate neighborhood of the roots of each tooth, from which a defensive system is built up to prevent the spreading of infection. Peridental infections, however, do sometimes result in extensive bone lesions and because these are usually chronic and not accompanied by any distinguishing symptoms, teeth associated with them are often treated for months by means of root canal medication without success. The jaws, therefore, are frequently seriously involved when the patient finally is sent to a roentgenologist or oral surgeon.

Ostitis.—Ostitis of a more extensive type develops often from periapical infections. When of the suppurative type, it is accompanied by violent acute symptoms, but more often it is of chronic character, developing from chronic periapical infection. Such granulating ostitis may involve large portions of the jaw and several teeth without causing much swelling or pain. A Roentgen picture of granulating ostitis is shown in Figure 13. Note the large, dark area of irregular outline, marked A.

Diffuse Osteomyelitis.—This is fortunately very rare, but when it occurs is a serious disease. It spreads, as a rule, from one side of the jaw

to the other and with the best of care it often takes months for complete recovery.

In one case such an infection started from an abscessed tooth, improperly treated. When the dentist finally extracted it the disease had already spread extensively as is indicated by the dark channels in the Roentgen picture extending throughout the jaw.

Periodontal Cysts.—These are found quite frequently. The writer has seen a large number during the last few years. They are caused by chronic abscesses containing epithelium. As their secretions accumulate they increase to enormous size, forming a large cavity in the bone, which sometimes reaches the size of a hen's egg. They nearly always contain pus. The bone itself is not infected, but is absorbed and sometimes becomes so thin that it can be bent when pressed with the finger. In the upper jaw cysts may encroach on the nasal cavity or develop inside the maxillary sinus a condition which is very difficult to diagnose. In the lower jaw they are found in the body of the mandible, as well as in the ramus. Periodontal cysts sometimes have apparently no connection with a tooth root. In such cases the offending tooth may have been extracted, the cyst having escaped notice at the time, or there may have been left in the jaw an epitheliated granuloma, which developed into a cyst later.

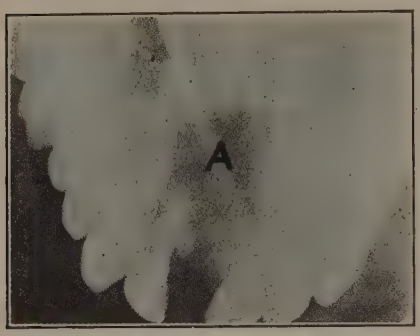

FIG. 13.—ROENTGEN PICTURE OF GRANULATING OSTITIS. This was taken after the left maxillary central incisor had been extracted and the pulp removed in the lateral incisor for the treatment of a condition.

The diagnosis of a cyst is easily made by means of Roentgen pictures. The cyst cavity appears as a black area on the negative with a light, but distinct, surrounding line, well illustrated in Figure 15.

Follicular Cysts.—Follicular cysts are, as the name implies, caused by an abnormal development of the dental follicle. They often contain an odontoma and are then called cystic odontoma. They are not caused by periapical infection but become frequently infected from a near-by abscessed tooth (Fig. 14).

Treatment.—The treatment in most cases is surgical. The importance of a correct diagnosis is illustrated by the following cases in which the true nature of the disease was not recognized.

Case of Granulating Ostitis.—The patient had soreness of the gums in the anterior part of the maxilla. The dentist first treated the central incisor and when the condition did not improve he extracted the tooth. Later the pulp of the lateral incisor was removed. Finally a Roentgen

examination was decided on and it revealed an extensive radiolucent area, indicating granulating ostitis (see Fig. 13).

Case of Diffuse Osteomyelitis.—The patient had had pain on the right side of the jaw for several weeks. He had had several teeth treated and afterwards extracted. There were very marked constitutional symptoms and the patient was in bed five days. When last seen by his dentist, extraction of the left mandibular third molar was advised. This was the only tooth remaining on that side. Examination showed swelling on the cheek and a fistula discharging pus into the mouth. The third molar was perfectly firm, but the incisors were tender on percussion. Temperature, 100. Pulse good. No severe pain. Roentgen examination of the jaw showed large pieces of bone, separated by dark shadows, indicating extensive osteomyelitis of the mandible, with several sequestra.

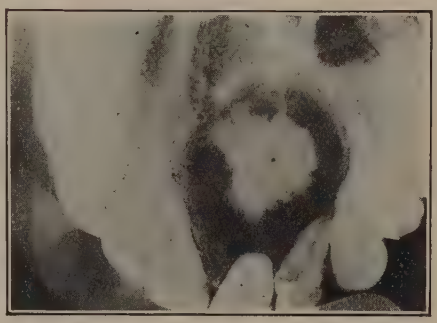

FIG. 14.—A SWELLING UNDER THE LIP SUPPOSED TO HAVE BEEN DUE TO INFECTION. Pulp of lateral incisor was removed. Roentgen examination reveals cystic odontoma.

Case of Cystic Odontoma.—The patient, a boy sixteen years old, had noticed a swelling under his lip for several months, the left maxillary lateral and central incisors being somewhat tender to touch. His dentist opened the lateral incisor, removed the pulp and treated the root canal. Whenever the root canal dressing was removed, a yellowish fluid escaped from the tooth. The root canal treatments failed to help the condition and the gum was lanced several times without result. When the boy was first brought to me for consultation, a Roentgen picture was taken, from which a diagnosis of cystic odontoma was made. Note the dark area with definite outline, indicating a cyst cavity in the bone. The radiopaque substance in the center of the cyst is an odontoma (see Fig. 14).

Case of a Bridge over a Cyst.—The patient had two teeth extracted and replaced by a bridge. She complained at various times of an inflammation of the gum under a bridge in the mandible. Her dentist had lanced the gum several times. On examination the bridge was found to extend from the second bicuspid to the third molar, and one of these teeth was suspected of causing the trouble. The gum around the bridge was hypertrophied, and pus could be pressed from a fistula. Roentgen examination showed that the two bridge abutments were perfectly healthy teeth with normal pulps. A large cavity in the bone between the two teeth presented in the Roentgen picture the typical appearance of a cyst. A diagnosis of infected radicular cyst was made. Apparently a tooth had

been extracted, leaving the cyst, which was not discovered during examination (see Fig. 15).

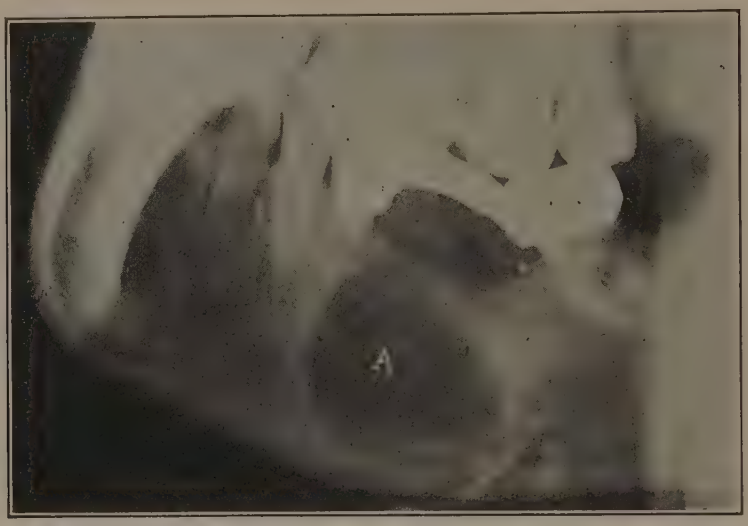

FIG. 15.—ROENTGEN PICTURE OF LARGE CYST (A). Patient complained of inflammation around bridge in lower jaw. Teeth had been extracted for treatment of an infection which was disturbing the patient. The large cyst (A) had been overlooked.

Infection of the Maxillary Sinuses.—Infection of the maxillary sinuses is quite frequently of dental origin and in many other cases diseased teeth become an important contributory cause. Careless instrumentation in connection with tooth extraction, or accidentally pushing an

FIG. 16.—UPPER JAW WITH THE OUTER CORTICAL PLATE REMOVED. Illustration shows the relation of the teeth to the maxillary sinus (A).

infected tooth root into the sinus, may cause acute maxillary sinusitis. Chronic dental infection, such as occurs on pulpless teeth, is, however, more frequently the etiological factor and generally results in chronic infection of the maxillary sinuses, with polypoid degeneration of the mucous membrane. This condition often develops without the patient's knowledge, and is discovered only in routine examination. If extensive diseased areas are seen in the Roentgen pictures of the maxillary molars and bicuspids, sinus disease should always be considered as a possibility, and Roentgen pictures of the head should be taken for investigation. On the other hand, in cases of sinus symptoms, or sinus disease, investigation of the teeth should not be neglected, and their condition must be diagnosed roentgenographically before any treatment is undertaken.

Treatment.—It should be remembered in connection with a probable dental cause that, if we see in a Roentgen picture a small area around a root, it does not necessarily mean that the dental condition is negligible, because in some cases there is not enough bone between the sinus cavity and the alveolar socket to form a large abscess cavity (Fig. 16). Such a condition is more liable to cause sinus infection than a tooth with an extensive abscess cavity well removed from the floor of the sinus. The treatment consists in extraction of the tooth, thoroughly removing all infected tissue from the floor of the sinus and, if a perforation has been made, to close the wound with sutures, after sterilization with tincture of iodin. The rest of the treatment should be from the canine fossa and the nose.

Dental Cysts Invading Maxillary Sinuses.—Periodontal cysts developing from the maxillary bicuspids or molars, or dentigerous cysts originating from misplaced tooth germs, often encroach upon the maxillary sinus. In many cases the cyst is so large that it fills the sinus cavity almost entirely. There is but a thin bony wall separating the remaining part of the sinus from the cyst cavity. This can usually be seen in the Roentgen picture.

GENERAL DISEASES CAUSED BY ORAL FOCAL INFECTION

The fact that until recently dentistry has been looked at as a profession apart from medicine is probably the reason why for a long time it was thought that infections connected with the teeth had no effect on the rest of the body. On the other hand, since the discovery of focal infection, a great many good teeth have been ruthlessly sacrificed on the evidence of a careless diagnosis. Better coöperation between the dentist and the physician is highly desirable. The patient who goes to the dentist with a story of some chronic disease would be greatly benefited by proper medical examination. The internists may be able to give the dentist valuable advice with regard to the general health of the patient on whom he is about

to perform an oral surgical operation and in the matter of selecting a suitable anesthetic. The examination of the teeth and oral tissues, however, should be performed by one qualified for this work who should not only be familiar with the technical procedures of dentistry but specially trained in oral anatomy and pathology. The reports from general roentgenologists are often very misleading. A dental consultant will generally take his own Roentgen pictures and will at the same time make a clinical examination which is indispensable for a correct diagnosis.

General or constitutional effects from acute dental infection as evidenced by fever, headaches, constipation and even delirium are easily recognized clinically, but in chronic infection the systemic effects may be taken care of by the protective forces of the body. When, however, the general resistance becomes lowered by debilitating disease, poor physical condition, pregnancy, exposure, or malnutrition, serious complications may gradually develop, so gradually that frequently the patient is not aware of the systemic disease until irreparable harm has been done. To show how different an effect the same disease may produce in a perfectly normal body and one in which the resistance has been lowered by chronic disease, the following observation of 2 patients made by Dr. McCrudden, of the Robert B. Brigham Hospital of Boston, may serve as an illustration.

The first, a woman with a perfectly healthy heart, Hospital Case No. 225, and the other, a patient with a weak heart, Hospital Case No. 211, both had the same amount of vaccine injected. The first patient, a well-developed and well-nourished woman, had been suffering from chronic arthritis for 21 months. Lungs, normal; heart sounds regular and of good quality. On February 20 vaccine treatment was begun. Injection of 75,000,000 typhoid bacteria with 100 c.c. of normal salt solution was made at 3.30 P. M. into the median basilic vein. She had a definite chill, which lasted 20 minutes, but there were no heart symptoms. Temperature and pulse curve shown on chart in Figure 450. By 9.30 P. M. these were perfectly normal. A second vaccine treatment of 100,000,000 bacteria, given 8 days after, produced a similar result.

The second patient, a woman aged 36 years, was admitted to the hospital for chronic arthritis. She had had measles, diphtheria and scarlet fever when a child; at the age of 12, Saint Vitus' dance, which lasted 2 years; 2 attacks of pneumonia when 15 years old and rheumatic fever 7 years previous to admission. Present illness had begun 18 months before, when she had noticed pain and stiffness in the knees. The joints of the fingers, elbows and shoulders then became involved. Present examination showed slight edema in ankles, teeth poor, glandular enlargement in submaxillary region on both sides. There was a systolic murmur of the heart, but no evidence of organic disease. At 4.15 one afternoon the patient received a vaccine injection intravenously of 75,000,000 bacteria. At 5 P. M. there were signs of reaction, chill, typical spasmodic shaking, but

no complaint of cold. She had marked cardiac symptoms at 9 P. M. Patient was dyspneic, cyanotic and coughing. Sputum was salmon-colored. Distress, dyspnea and headache lasted until about midnight and the next day there was still tenderness and palpitation over the precordia (Fig. 17).

These two cases illustrate the different effect on two patients of a small and limited amount of toxin. The healthy patient, in this case the one with the strong heart, can easily take care of a slight infection, while another patient not in perfect health may suffer from a similar cause most severely.

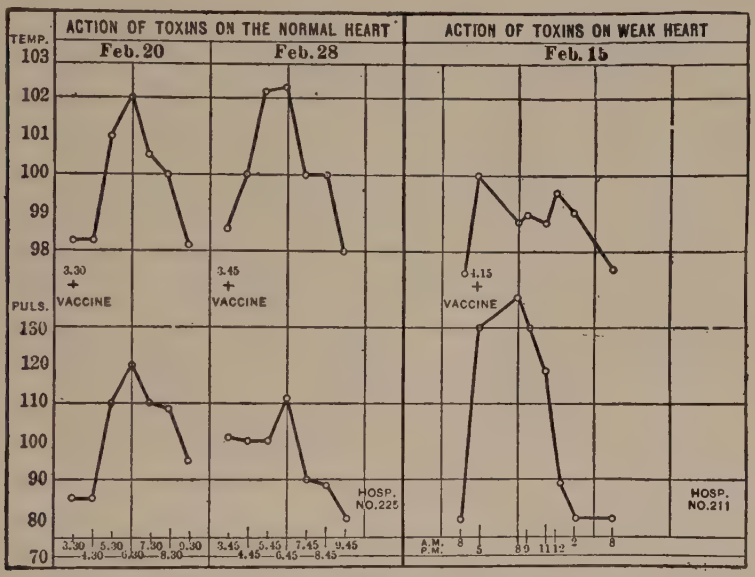

Fig. 17.—Action of Toxins on the Weak and Normal Heart. (Courtesy of Dr. McCrudden.)

Oral Foci of Infection.—Systemic infection may be caused by dental or oral lesions but it is a mistake to spread the impression that diseases of the mouth and teeth always play a predominant part. The focus may be found in any other part of the body, the nose or throat and adjacent sinuses, the alimentary canal and genito-urinary system. Systematic examination is therefore of greatest importance and when infections are found in the oral cavity it is still necessary to determine whether they represent an original focus, or one of several from which bacteria have migrated to other organs, or in which toxins have been produced and absorbed, or whether the dental infections and the systemic conditions are simply coexistent and not directly related to each other. These questions must be considered individually for every case.

In a patient suffering from a disease which has nothing to do with oral

infection, such a condition may nevertheless become a considerable burden on the body, as has already been discussed. The continuous fighting of the infection and elimination of the poisons produced must be a great tax on the organs whose function it is to combat disease. Therefore, for this reason alone it is important to search for and eliminate disease conditions in the mouth in order to raise the resistance and improve the patient's general health.

The various lesions which may cause disease in other parts of the body may be divided into those which discharge pus into the mouth and those where there is no outlet and the mode of transportation of bacteria or toxins is that of metastatic infection. Among the first group belong periapical infections with fistulæ, oral sepsis from all kinds of unsanitary conditions, especially those connected with poorly fitting crowns and bridges and pyorrhea pockets discharging into the mouth. The pus mingles with the saliva and food during mastication and causes infections of the throat. It reaches the stomach and intestines, giving rise to diseases of the mucosa of the alimentary canal. For a long time the acids of the stomach have been looked upon as destructive to such bacteria, but Smithies, in a microscopic examination of gastric extracts from 2,406 different individuals with "stomach complaint," showed that, irrespective of the acidity of such gastric extracts, bacteria were present in 87 per cent. Hunter says there is a limit to the power of the stomach to destroy such organisms. Even in health it is never complete and is solely due to the presence of free hydrochloric acid; this power, however, becomes progressively weakened, when through any cause an increased and continuous flow of pus organisms is associated with a diminished and continually lessening acidity of the gastric juice.

Among the second group belong the blind abscess or dental granuloma, pulp infection, the less frequent bone infections and infectious cysts. These conditions may give rise to a variety of special and general diseases under favorable circumstances. The most common are those otherwise unexplainable obscure symptoms of toxemia, such as fatigue, disproportionate to the slightest exertion occasioning it, inability to do, mentally or physically, the accustomed day's work, benumbed mental activity, requirement of an abnormal amount of rest, loss of weight, grayish or sallow skin, and a rise of temperature in the afternoon or evening. A person who is perfectly healthy may be able to eliminate a certain amount of infection, but sooner or later serious results are apt to occur. Lowering of the body temperature by cold or wet may give rise to more or less vague rheumatic symptoms such as myositis, arthritis or neuritis. Cases of acute multiple arthritis from dental infections are not uncommon and generally improve rapidly after removal of the focus. In chronic infections, especially arthritis of long standing, the results are not so gratifying. The joints may present tissue changes which are beyond repair from an anatomical point

of view. The removal of the focus, however, usually relieves symptoms of pain and swelling and prevents reinfection from this cause. Lymphangitis and lymphadenitis of the submaxillary and submental lymph glands are often caused.

Dr. Crosby Greene in a symposium "The Teeth in Relation to the Specialties in Medicine" states that there is no question as to the spread of infection from foci in or about the teeth to the throat by continuity. Retropharyngeal abscesses are often the result of acute infections connected with lower third molars. The relation of narrow arches to the formation of adenoids and of dental infection to disease of the maxillary sinuses has been dealt with at length. Ear infections, such as acute otitis media or chronic purulent inflammation of the middle ear and tympanum, may be caused by direct invasion through the eustachian tube, or the infection may be transported by the circulation. Pain in the ear, so-called otalgia dentalis, is frequently only a reflex pain from some cause in or about the teeth.

Children are frequently victims of focal infection causing grave and sometimes irremediable conditions, such as endocarditis, nephritis and acute inflammation of the joints. Acute or chronic lymphadenitis is also a common occurrence in children and often caused by the teeth.

Wells stated, in the same symposium, that the committee for investigating the cause of iritis and iridocyclitis of the Academy of Ophthalmology and Otolaryngology reported at the last meeting, after two years' work, the collection of 90 cases, only 40 of which had been examined with sufficient detail to meet the requirements. Of these about 20 per cent were found to be due to focal infection from teeth and tonsils. Benedict of the Mayo Clinic says the method of transmission may be due to direct extension through bone, to direct extension along the periosteum or through transfer of organisms from the focus through the blood-stream, which possibility is well demonstrated by the laboratory experiments of Rosenow.

Professor W. T. Lee writes that it has been unquestionably proved that oral infections are direct or indirect factors in the causation of some skin diseases, of which he specially mentions furunculosis, acne vulgaris of the pustular type and other pustular diseases of the skin. While some dermatologists have been very enthusiastic in their advocacy of focal infection as the cause of many skin troubles, it is his opinion that, as time has passed, the feeling has developed, that too much stress has been put upon focal infection as the chief or exclusive cause of certain dermatoses.

Dr. F. Gorham Brigham, who presented the relation of internal medicine to the teeth, states that diseases of the cardiovascular system, including the large group of arterioscleroses, are greatly benefited by the curing of oral disease, in many cases rapidly progressing conditions being checked almost as by magic.

Treatment.—When searching for foci of infection in the mouth it is of great importance to have the patient examined clinically as well as roentgenographically. A complete Roentgen study of all the teeth should be insisted upon, including also the edentulous spaces, where broken roots, bone abscesses or cysts occur quite frequently. If any of the teeth connected with the maxillary sinus are infected, the nasal and accessory cavities should also be roentgenographed. A departure from a thorough routine examination often leads to regrettable oversights.

Positive statements cannot be made with absolute certainty as to the probable benefit of removing the focus. The secondary lesion or disease may be of such long standing that the removal of the original focus has but little effect, or the tissue changes are so extensive that restoration to the normal cannot be expected. The best results are obtained in cases of short duration, and especially in those where the secondary disease is due to toxemia rather than to bacterial migration. After finding oral lesions in a patient who complains of symptoms caused by diseases conceded to be due to focal infection, the patient should also be carefully examined for foci in other parts of the body.

In patients suffering from some chronic disease, or whose resistance is lowered, radical dental treatment is generally indicated. It is perfectly justifiable to be radical in such cases, not only with diseased, but even with suspicious teeth, although they may not be the direct cause of the general condition. A perfectly healthy body can take care of a certain amount of toxin, but the same amount in a patient suffering, for example, from subacute endocarditis may produce serious results. McCrudden states that "in chronic disease the hopeful therapeutic measure lies in improving the functional efficiency of the body and building up the general health. To further this end it is important to remove all necrotic tissue, because the organs whose function it is to combat disease must be freed from any additional burden."

Another aspect of this problem is the question as to whether it is perfectly safe for an otherwise healthy patient to retain infected teeth which, on account of their chronic character, cause no local disturbance, but which show infectious processes at the ends of the roots when roentgenographed. While there is little doubt in most cases as to what should be done with badly infected teeth, there are, nevertheless, cases where we should like to recommend and try more conservative methods if we could be sure that no systemic absorption is taking place. Where apical necrosis and root absorption of long standing are discovered in the Roentgen picture, indicating clearly that nature wants to eliminate, extraction is indicated, from a purely dental point of view. No one who has studied the tooth and bone pathology of old pus-soaked teeth, or who has experienced the odor of one which has been removed, would ever hesitate to recommend extraction, simply for the sake of cleanliness. But in cases of short standing, es-

pecially in younger patients, treatment and retention of a tooth would seem advisable if the roentgenographic indications are favorable to root-canal work.

A great deal has been heard lately about ruthless extraction of teeth and the writer frequently sees patients who were advised to have all their teeth removed without a Roentgen diagnosis having been made. Equally radical and unnecessary is the so-called surgical removal of the teeth which has been advocated lately. The method consists of cutting a flap on the side of the gum, chiseling the bone away and then removing the tooth laterally, performed by many with ether anesthesia in the hospital. Such extreme procedures are not necessary for the ordinary case and should be reserved for cases of difficult extraction. The infectious granulation tissue of the chronic abscess can be removed easily from the socket after the tooth has been extracted, injury of the bone should be avoided when this is done and, if the alveolar margin is injured accidentally, or a small piece broken off, it is a simple matter to smooth the sharp ridges and projecting pieces of bone.

In cases of focal infection, especially when the patient's resistance is lowered, proper judgment should be used in determining the number of teeth that are to be removed at one time. It is not only the shock of the operation which must be considered but rather the fact that new channels are opened for absorption of bacteria and toxins. When a local anesthesia is used these effects of the operation are very often erroneously blamed on the drug employed. The removal of a large number of infected teeth at one time is known to cause under certain circumstances very alarming constitutional symptoms and cases are on record where wholesale extraction caused the death of the patient. Extraction at intervals, which should be from six to eight days, is on the other hand of therapeutic value, inducing a similar effect as that of repeated vaccine treatment.

DENTAL AND TRIGEMINAL NEURALGIA

The extensive area of distribution of the trifacial nerve and its frequent communications with other cranial nerves and the sympathetic system explain the clinical manifestations that pain and irritation, originating from some dental or oral cause, may be referred to very distant parts of the face and head (Fig. 18).

Dental Neuralgia.—Such pain may be continuous, intermittent or periodic; it may be intense, sharp, throbbing or dull; and it may be a sensation of obscure, indefinable pressure. The suffering that goes with these conditions is often intense and, if of sufficient duration, wears the patient out. It sometimes results in serious nervous disorders, such as insomnia, melancholy and epilepsy.

The cause is generally difficult to ascertain and it is necessary to make very careful study of the history and symptoms, combined with physical

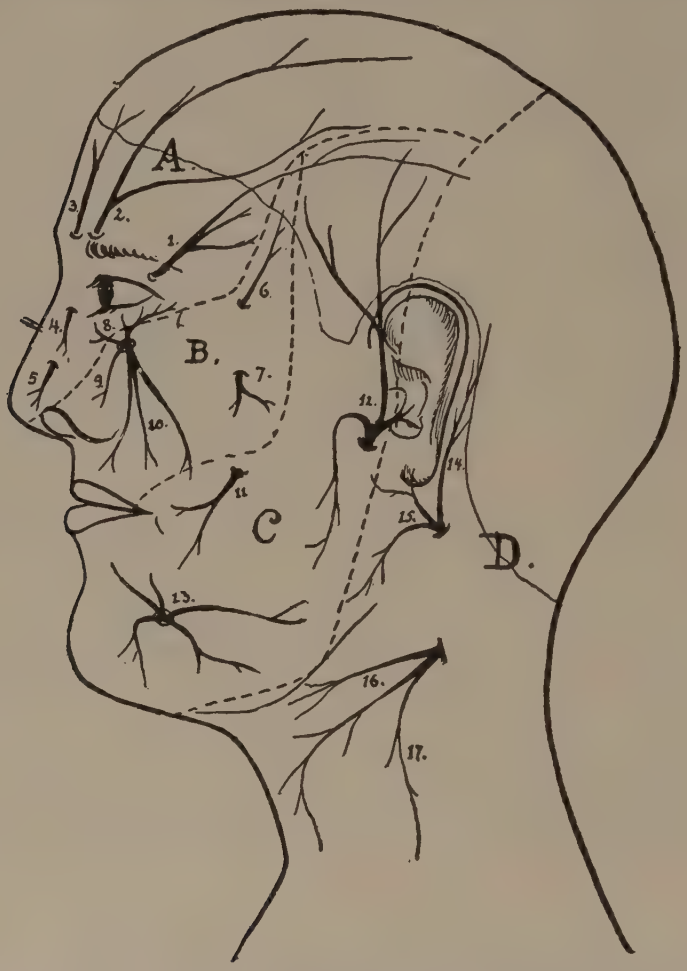

FIG. 18.—DISTRIBUTION OF THE V NERVE ON THE OUTSIDE OF THE FACE. Area A supplied by first division of V nerve. B supplied by second division of V nerve. C supplied by third division of V nerve. D supplied by cervical nerves. 1, lacrimal N. 2, supra-orbital N. 3, supratrochlear N. 4, infratrochlear N. 5, external nasal N. 6, zygomatic-temporal N. 7, zygomatic facial N. 8, 9, 10, palpebral, nasal and labial branch of infra-orbital N. 11, buccinator N. 12, auriculotemporal N. 13, mental N. 14, 15, posterior and anterior great auricular N. 16, 17, superior and inferior cutaneous coli. N.

examination and tests and a careful Roentgen examination, not only of the teeth on the affected side by intra-oral films, but also of the entire side of the face.

Undetected dental caries, with or without pulp involvement, is one of

the frequent causes. Caries under a filling, or on the surface of a tooth beneath the gum, may be discovered by means of a Roentgen picture. First cold and later heat will bring on an attack, but it may be entirely independent of any known cause.

Dental neuralgia is often attributed to pulp calcifications and pulp nodules. The writer has seen several cases of this type. One should, however, rule out other possible causes before deciding to sacrifice the pulp of a tooth, as these pulp nodules are very often simply coexistent and have nothing to do with the cause of the pain.

The dentinal branch of the nerve, before entering the tooth apex, often becomes inflamed, especially in teeth from which the pulps have recently been removed, or in cases of periapical infection. Treatment by apicoectomy has been successful in several such cases.

Chronic parietal abscesses, especially between the three roots of a maxillary molar, where recognition is difficult even with good roentgenograms, may cause prolonged suffering. The teeth may be vital and not sensitive to percussion. Pyorrhea, especially if caused by poor restoration, may be found to be at the root of a neuralgic affection.

Unerupted and impacted teeth are very commonly the cause of obscure neuralgia expressed in varying ways. The neuralgia may be due to pressure against the obstructing tooth or bone, sometimes causing pressure absorption and pulp exposure on the tooth against which they lie. Pressure of developing roots against the nerve trunk is more frequently the cause of the trouble. Impacted teeth may lie dormant for a long time and then suddenly start to exert pressure. This period of rest and activity is generally repeated at irregular intervals.

Neuritis of the Alveolar Nerves.—The larger peripheral nerves in the bony canals become at times inflamed from irritation or infection of a tooth, or after extensive surgical interference. Such a neuritis generally lasts several weeks and is sometimes associated with paresthesia of the part supplied anterior to the injury. This is, of course, only temporary and is due to pressure exerted by the wall of the nerve canal in the bone upon the nerve trunk increased in size from the inflammation.

Otalgia Dentalis.—The tympanic plexus is connected with the second division of the fifth nerve by means of the sphenopalatine, or Meckel's ganglion, via the great superficial petrosal nerve. The third division communicates through the small superficial petrosal nerve and otic ganglion, which also gives a branch to the tensor tympani.

Pain from an infected pulp in a tooth, from a surgical wound in the mouth or from an impacted tooth is very often referred to the ear via the nerve connections just described, causing an otalgia without local ear disease.

Trigeminal Neuralgia (Major) or Tic Douloureux.—This is not caused by any condition of the teeth. Its etiology and pathology are un-

known. Any of the pathological conditions described may be coexistent with it, but their removal will never cure a real trifacial neuralgia. If this were borne in mind and the symptoms of the disease, which is quite different from a dental neuralgia, recognized in time, many of these poor sufferers would be spared the loss of valuable teeth.

The characteristic symptoms which differentiate trigeminal neuralgia from the foregoing type are well described by Silverman. The patient is usually middle-aged, or older, complains of sharp lancinating pains, or severe burning flashes which shoot through some area supplied by any of the branches of the trigeminal nerve. The subject has suffered for a year or more, he may have a premonitory aura not unlike that found in epileptics. When such an aura is present the patient can sometimes ward off the attack. The alteration of facial expression accompanied by a ghastly stare is very characteristic in these cases. The patient may explain that a tooth, or some other area supplied by the fifth nerve, will, when touched, cause severe paroxysms of pain. Talking or laughing is likely to bring it on. Washing, rubbing, shaving, powdering, or having the bed covers touch the area is sufficient to elicit the pain. In fact a draft of air or the alighting of a fly may bring on an attack. One characteristic which is paramount, however, is that the patient will invariably state that the pain is the most excruciating of all pains.

It is often difficult to convince patients suffering from trifacial neuralgia that the tooth in which they think the trouble is located is not the cause of the pain. This is true even when they have had one after another extracted. Always it is the next tooth in line, until all are gone, and still the pain persists. The patient is then without teeth and, on account of the disease, or its treatment (alcohol injection or nerve evulsion), finds it more difficult to wear a denture than the normal person.

Treatment.—In dental neuralgia and otalgia dentalis the removal of the cause will in most instances give prompt relief of the symptoms. Many times there are several conditions found in different teeth, when it is possible to make a diagnosis by eliminating one tooth or nerve branch after another by means of local anesthesia (see Thoma, Oral Anesthesia). In major neuralgia, alcohol injections or evulsion of the terminal nerve branches will in a great many cases give very satisfactory results. The writer has been very successful in cases affecting the infra-orbital or inferior alveolar nerve with the method of evulsion of the nerves by means of an intra-oral operation.

PREVENTION OF DENTAL DISEASES

Every effort should be made to prevent dental infections and this means frequent examination so as to discover and treat the early stage of

such diseases as gingivitis and dental caries, before irreparable harm has been done. Until certain errors in our diet have been radically changed, prophylactic treatment at home as well as by the dentist at regular intervals is necessary successfully to combat dental disease. This means education of the public along these lines, careful and repeated instruction of the patients in oral hygiene and the selection of food which furnishes all the constituents necessary for the formation of good bone and hard and solid teeth. Such measures should be begun as early as possible. Every child has the right to be protected from preventable diseases and to be started off in life with healthy teeth. It is the dentist's duty, therefore, to encourage the application of his present knowledge and skill, but the coöperation of the physician is very much needed as he directs the diet of the expectant mother and takes care of the child during the first years of its life, which, as we have seen, are the most important for tooth development.

REFERENCES

Baker, Lawrence. Further Evidence As to the Influence of the Forms of Occlusion, and the Development of the Bones of the Skull, Items of Interest, xxxviii, 488, 1916.

Brigham, F. Gorham. Teeth in Relation to Internal Medicine, Dental Cosmos, lxiv, 540, May, 1922.

Editorial, Lancet, Jan. 8, 1916.

Greene, D. Crosby. Teeth in Relation to Disease of the Nose and Throat, Dental Cosmos, lxiv, 530, May, 1922.

Grieves, C. J. Defects in Rats on Defective and Deficient Diet, Journ. Am. Dent. Ass., 467, June, 1922.

Howe, Percy R. Further Studies of the Effect of Diet upon the Teeth and Bones, Ibid., 201, March, 1923.

Hunter, William. Oral Sepsis as a Cause of Disease, London, Paris, New York and Melbourne, Cassel & Co., Ltd., 1911.

——— Pernicious Anemia, Charles Griffin & Co., London, 1901.

Lee, Wesley T. Teeth in their Relation to Diseases of the Skin, Dental Cosmos, lxiv, 532, May, 1922.

McCrudden, F. H. The Treatment of Chronic Disease as a Problem of Applied Physiology, Boston Med. and Surg. Journ., No. 2, clxxv.

Neumann. Volkmann's Samml. klin. Vortr., No. 172, 1897.

Rogers, Alfred. Arch. Pediat., March, 1922.

Rosenow, E. C. Studies on Elective Localization, Focal Infection with Special Reference to Oral Sepsis, Journ. Dent. Research, i, 204, 251, 1919.

Sherman, H. C., and Hawley, E. Calcium and Phosphorous Metabolism in Childhood, Journ. Biol. Chem., 398, Aug., 1922.

Silverman, S. L. Trigeminal Neuralgia, Journ. Am. Med. Ass., lxxvii, 1802, 1921.

Smith, H. Carlton. Chemistry for Dental Students, 4th ed., ii, Wiley & Sons, New York, 1924.

Smithies. Cited from May, C. H., Mouth Infection as a Source of Systemic Disease, Journ. Am. Med. Ass., lxiii, 2025, Dec., 1914.

Thoma, Kurt H. A Histo-pathological Study of the Dental Granuloma and Diseased Root Apex, Journ. Nat. Dent. Ass., Oct., 1917.

——— The Condition of the Bone in Cases of Dental Granulomata, or Chronic Alveolar Abscesses, Items of Interest, June, 1918.

——— Oral Anesthesia, 2d ed., M. C. Cherry, Boston, 1920.

——— Oral Roentgenology, Lea & Febiger, Philadelphia and New York, 1922.

——— Teeth, Diet and Health, The Century Company, 1923.

Wells, David W. Teeth in Relation to Diseases of the Eye, Dental Cosmos, lxiv, 524, May, 1922.

CHAPTER XXVIII

DISEASES OF THE PHARYNX

BURT R. SHURLY AND GEORGE E. SHAMBAUGH

PHARYNGITIS

BURT R. SHURLY

Acute Nasopharyngitis and Pharyngitis or Faucitis.—Acute nasopharyngitis and pharyngitis or faucitis occur usually with involvement of the nasal passages, tonsils, uvula, or larynx. These acute inflammations are familiarly known as "colds." They may develop as independent affections, or it may be necessary to treat an attending digestive disorder as well, as the acute process may be recognized as really an exacerbation of a chronic inflammation. The treatment by a mild calomel purge, followed by a saline laxative, may be entirely efficacious. If abnormal temperature or dysphagia be prominent symptoms then salol with acid acetyl salicylate, 5-gr. doses each, will give prompt relief. Tincture of aconite or phenacetin may well be chosen instead.

In cases with considerable edema of the mucous membrane and glandular involvement an irrigation or douche, by means of a fountain syringe, with a solution containing a teaspoonful of pulv. antiseptic comp. to a quart of very hot water is a valuable remedy. The nozzle of the syringe or douche should be placed well back in the throat and the solution allowed to bathe the inflamed area before flowing out of the mouth cavity into a receptacle. An astringent and antiseptic gargle consisting of carbolic acid, 10 minims, with pulverized alum, ¼ teaspoonful, in a glass of water gives great relief. The use of orthoform, or mentholated lozenges, often affords great comfort. Pellets of cracked ice allowed to dissolve in the mouth lessen congestion. An ice collar is both grateful and useful if the glandular swelling produces pain, although hot applications may prove more soothing in some cases. If the patient is under observation early in the attack an application of argentum nitrate (gr. xx to ℥i) to the pharynx and 10 gr. to the ounce to the nasopharynx will have prompt astringent and analgesic effects upon the congested area. When these acute conditions are attended by uvulitis the powerful astringents, such

as tannic acid, ferri-alum, or iron persulphate, may be applied. If these measures fail the sides of the uvula may be incised. Adrenalin chlorid (1:1,000), or cocain and antipyrin (of each 2½ per cent), will afford temporary relief. The use of a stock vaccine when the bacteriology of the prevailing epidemic is known has been suggested. The diet should be liquid or simple and non-irritating.

It is well to bear in mind that these acute inflammatory conditions are frequently nothing more than an initial demonstration of some constitutional infection or dyscrasia such as measles, scarlet fever, varioloid, pertussis, diabetes mellitus, diphtheria, tonsillitis, gout, acute articular rheumatism, typhoid fever, erysipelas, pernicious anemia, or the onset of tuberculosis. Therefore constitutional treatment must be administered.

Frequent recurring "colds" require a special investigation as to the etiological factors at work. Onsetting tuberculosis, pathologic tonsils and adenoids and particularly sinus disease have this history. The lowered resistance to infection requires a definite explanation for each individual. A thorough examination of the nasopharynx is made only by the specialist as a rule, yet here is the key to treatment of almost all extensions of infection or so-called catarrh to the middle ear. Postnasal irrigation with normal saline or mild alkaline antiseptic solutions will often prove of great value especially in children unable to clear the nasopharynx with suction or blowing. For postnasal irrigation in acute streptococcic or influenzal infection the writer has found the following of value:

℞	Bismuth subcarb.	℥i
	Liq. hydrastis (colorless)	℥ii
	Boroglycerid	℥i
	Aqua distillata q. s. ad.	0i

Also an eye-dropper full of argyrol, 20 per cent, through the nasal passages. Sinuses, especially the antrum of Highmore, even in children, must be drained by suction or washed by puncture or irrigating tubes as necessary.

Chronic Nasopharyngitis and Pharyngitis.—The local inflammation of the pharyngeal mucosa is frequently a reflection of some important constitutional dyscrasia, such as focal infection, rheumatism, gout, syphilis, tuberculosis, the anemias, renal and cardiac lesions, digestive disorders, and intoxications, or the excessive use of alcohol and tobacco. All of these, especially the latter habits, must receive prompt and appropriate attention and treatment. The use of the voice must be investigated and regulated. Questions regarding clothing, exercise, occupation, and bathing must receive attention and proper advice. High blood pressure, if present, should be modified by giving epsom salts before breakfast, or other appropriate laxatives and remedies. Chronic nasopharyngitis is

frequently the result of neglected adenoids. If remnants of this enlarged or altered tissue be present they should be destroyed or, better, removed. The prevention of acute rhinitis should be urged, and radical treatment adopted at the onset of each attack. Internally the administration of the syrup of the iodid of iron or hydriodic acid may prove of value. Locally, sprays and gargles afford comfort and relief to the patient. Where painful deglutition exists a hot throat douche, or a nasal douche of a solution of pulv. antiseptic Co. (℥i to the quart of very hot water), may be applied. It is grateful and cleansing. When the mucus is particularly tenacious a strong saline solution or equal parts of soda biborate and boric acid (a teaspoonful to a glass of hot water) is a readily prepared and useful solution. In addition, the posterior, pharyngeal, and nasopharyngeal wall should be painted daily with a pigment compound of iodin, gr. x; potassium iodid, gr. xx; and glycerin, ℥i; also a solution of silver nitrate, gr. x to ℥i, should be applied once or twice a week. When a granular pharyngitis or chronic folliculitis exists these should be treated by touching the top of each hypertrophic zone with a galvanocautery tip at white heat, or with fused nitrate of silver. When the blood-vessels leading to the follicles are large and tortuous they should be cut off by touching them lightly with the galvanocautery electrode at a point in the middle of their course.

Among the astringents of value may be mentioned the sulphocarbolate of zinc, gr. x to ℥i; alumnol, gr. x to xx; or a 20 per cent solution of argyrol. The severe types of chronic pharyngitis will not respond to remedial measures until complete surgical methods are adopted, as necessity requires. It is also true that surgical procedure is frequently chosen too hastily, and may thus be harmful. The tonsils may be completely enucleated in some cases, after which a modified method of treatment to the pharynx may prove sufficient. Anterior or posterior hypertrophies or any marked pathologic condition should always be removed. A deflected septum when actually obstructive should be resected, and spurs, ridges, or excrescences should be removed surgically if necessary. Adenoid vegetations are especially a source of recurrent infection, in which event adenectomy only will afford relief in such cases. Sinus disease is probably responsible for more chronic nasopharyngitis than any other etiological factor. Transillumination and X-ray aids should be used with Hayes' pharyngoscope in addition to the usual methods to determine the extent of the infection.

Chronic Pharyngitis.—This disease in its various pathologic conditions demands a careful investigation of the nose, nasopharynx, and accessory side cavities to determine and relieve the etiologic factors contributing to the chronic pathologic changes.

Operative procedure should be instituted to correct nasal obstruction and restore good drainage. The use of alcohol and tobacco should be

prohibited or greatly curtailed. Spirituous liquors particularly are irritating and develop chronic hypertrophy.

The nose may be washed with one of the agreeable and efficient alkaline solutions. A small rubber syringe or glass douche may be recommended for the purpose with careful instructions to tip the head to the opposite side when each nasal passage is slowly irrigated. The eustachian tubes are not in danger when proper position and muscular control are attained.

Hypertrophied follicles should be obliterated by a galvanocautery tip at cherry-red heat. Five or six follicles may be cauterized at a sitting by gently sinking a fine-pointed electrode into the center of each follicle. Four per cent cocain will suffice to produce good local anesthesia. Hypertrophy of the lateral walls may be promptly reduced by the same process. A suitable electrode may be chosen for this application. Nitrate of silver (xx to xxx gr. to the ounce), or argyrol, 20 per cent, should be applied at indicated intervals to relieve mild forms of chronic pharyngitis. A gargle of alum, gr. v, potassium chlorate, gr. xv to the ounce of water, or a solution of alum, gr. viii, ac. carbolic, min. ii, glycerin and water to an ounce will add greatly to the comfort of the patient. Menthol or red gum lozenges are used with advantage. Gouty and rheumatic subjects, and all cases of pharyngitis secondary to systemic disease should receive a carefully prepared diet, a morning saline, and appropriate systemic treatment.

Pharyngitis, secondary to tonsillitis, should be relieved by tonsillectomy.

Atrophic Nasopharyngitis.—In atrophic nasopharyngitis the crusts are often removed with the greatest difficulty. Hydrogen peroxid will prove valuable in cleansing a space that resists the application of a post-nasal douche. The methods of treatment used in the nasal passages are equally efficacious for the nasopharynx. A change of climate is often of advantage. Some cases do well in a moist, warm climate. The accessory sinuses should be carefully investigated, and drained when necessary (see Atrophic Rhinitis).

Acute Retropharyngeal Abscess.—This disease generally affects infants and children. It is frequently mistaken for spasmodic croup or laryngeal diphtheria in cases attended by edema of the larynx. Adults may be affected. Digital examination of the oropharynx and laryngopharynx will reveal the developmental stage and location of the abscess. The chief aim is to evacuate the abscess as soon as possible. Pointing is usually present when the diagnosis is made. Medical methods of treatment are of little value except during convalescence. The internal method of incision should be chosen unless a communicating cervical abscess is found or the condition is probably tuberculous.

The following is the method of incising internally: The patient is prepared according to the method of intubation. A sheet is firmly pinned

around the body of the infant, in this manner holding the arms firmly at the sides. An assistant seated in a straight back chair firmly holds the body and legs of the child, while a second assistant holds the head and mouth gag in position. The operator, standing in front of the patient, depresses the tongue firmly with a tongue depressor until the abscess is exposed. A bistoury, with the blade covered by adhesive plaster, so as to leave only half an inch of the point exposed, is inserted into the abscess. The incision is made longitudinally from above downward, inclining toward the median line. The assistant is instructed quickly to turn the infant forward face down as soon as the incision is made, so that pus may run from the mouth. When the abscess is pointing below the line of vision it may be successfully evacuated by the finger nail of the index finger. The writer has opened many cases of retropharyngeal abscess by this method that went on to speedy recovery.

The use of chloroform or ether should be avoided if possible. In cases that require the external operation general anesthesia may be adopted without hesitation.

Acute Uvulitis.—Inflammatory processes that involve the uvula are usually attended by similar pathology of the surrounding tissue. A troublesome edema is frequently associated with peritonsillar abscess. This condition is relieved by scarification or multiple puncture with a sharp-pointed scissors. Hot astringent gargles, preferably alum (¼ teaspoonful to a glass of hot water) or a spray of alumnol, 10 to 20 gr. to ℥i, are valuable. Hot irrigation with alkaline solutions from a fountain syringe promotes a reduction of edema. Ballinger recommends a 500 candle-power leukodescent lamp to the neck at the angle of the lower jaw, passed back and forth for fifteen to thirty minutes, and held at a distance of eighteen inches. Lozenges of krameria or red gum, an ice collar, and chipped ice served at intervals add to the comfort of the patient.

When the congestion continues or ulceration develops an application of silver nitrate, 60 gr. to the ounce, hastens recovery. General as well as local treatment is required. Temporary relief may be obtained by the application of 1 : 1,000 adrenalin solution. When these measures fail the tip of the uvula may be excised and the exudate allowed to drain out.

Hypertrophy of the Pharyngeal Tonsil or Adenoid Vegetations.—The development of adenoid vegetations in early infancy and childhood demands prompt attention by the family physician. A pathologic condition of the nasopharyngeal space is responsible for more complications in the infectious diseases of children than any other anatomic region. The nasopharyngeal catarrhs of adult life are largely the result of neglected adenoids and acute infections into the sinuses or middle ear attending this condition during the developmental period.

The treatment of adenoid vegetations may be both local and general. The indication for local treatment is the relief of nasal obstruction. This

should be accomplished by surgical measures at the earliest possible moment. This is one of the most successful operations in the field of rhinology or laryngology, and should be performed with great thoroughness.

Adenoids are extremely common in children from two to eight years of age, and may persist into and through adult life. The old idea of letting the patient outgrow this condition, which is still accepted by some practitioners, should be most severely condemned.

The nasopharyngeal space may be low and broad, high or narrow, or greatly deformed by bony projections, especially in the median line of the roof, or in the region of the cervical vertebræ. Patients with severely crowded teeth and high arched palate should receive continuous and painstaking care by the orthodontist. The jaw may be spread and the crowded teeth gradually forced into proper alignment. This procedure may so affect the floor of the nose that additional air capacity may be obtained.

Innumerable remedies in the form of sprays, applications, and internal medication have been advocated for the relief of adenoids. Fowler's solution, the syrup of the iodid of iron, cod-liver oil, and potassium iodid have been lauded in the various textbooks. Iodin in formulæ of various kinds has been highly recommended. The fact has been demonstrated, however, that these remedies are practically worthless, and valuable time may be lost unless proper surgical methods are instituted for the complete removal of the hypertrophied lymphoid tissue.

Until operation can be performed, palliative measures may be adopted. Adrenalin ointment or solution, 1 : 10,000, followed by a warm saline irrigation with an eye-dropper or syringe, will afford great relief to infants especially. This may be followed by a spray of menthol, gr. v to the ounce of liquid petroleum.

Within the realm of laryngology it would be difficult to mention an operation followed by the satisfactory results that come from adenectomy. The relief of symptoms and probability of recurrence are generally in a direct ratio to the thoroughness with which this operation is performed.

It is important to examine carefully each patient and determine all causes of nasal obstruction. The promise of complete and speedy relief by operative procedure cannot be offered when deflected septa, high-arch palate, hypertrophied turbinates, polypi, sinus disease, enlarged tonsils, and congenital malformation exist. Open mouth breathing may continue after operation and require a special apparatus for holding the lower jaw in place until a habit of normal nasal respiration can be acquired.

The technic of adenectomy is comparatively simple, yet considerable dexterity is required to perform a complete operation. The beginner meets with many puzzling questions he must settle. Many hundred varieties of instruments are on the market that are recommended for the

operation. The majority of them are worthless to the beginner. Certain principles may be outlined in establishing a satisfactory method of procedure.

The American practitioner stands preëminently for the comfort and welfare of the patient. He administers ether on account of its safety. Selected cases may require a departure from this rule, and the anesthetic chosen may be nitrous oxid. Chloroform is unquestionably dangerous, as statistics have shown. The writer has discarded it entirely, although many operations have been performed without a fatality.

The anatomy of the nasopharyngeal space should be constantly borne in mind. A digital exploration will determine any peculiarity in the location of the hypertrophy. The mouth should be held open with a reliable mouth gag and the tongue held with a suitable depressor. A Gottstein curet should be passed in the median line behind the uvula and soft palate to the most anterior portion of the roof of the nasopharynx. It is important that the cutting edge should engage the hypertrophy at its upper anterior border. A sweep of the very sharp blade across the roof and down the posterior wall in the median line will remove the central mass of tissue. Care must be taken not to wound the tissue at the eustachian eminences when succeeding lateral sweeps are made. All growths in the fossæ of Rosenmüller should be removed with a suitable curet or the aseptic finger nail. Hypertrophy along the posterior wall may be removed with a right-angled curet. The space should be examined digitally and any remaining tissue removed. A piece of gauze wrapped about the index finger will bring away retained shreds. A sea sponge of ice water is held at the root of the nose to control hemorrhage.

The patient is put to bed and turned on the side to allow the blood and secretion to drain out. Unless signs of sepsis develop, no irrigation of the nose is required. A spray of adrenalin (1:10,000) or albolene may be used occasionally for the comfort of the patient. Excessive hemorrhage is exceedingly rare. It may be controlled by packing the nasopharynx with adrenalin and alum-soaked gauze, thromboplastin or prepared bismuth gauze.

The question of the regrowth of adenoids deserves attention. In many instances where a return of the original symptoms of hypertrophy have taken place, the operation was not thoroughly done. Care should be taken to remove all adenoid growth in the interior and upper angle of the vault of the pharynx. Many instruments are so imperfectly constructed that the sweep of the curet does not include this offending tissue. It is true, however, that in older children (over three years) a small percentage of cases will show recurrence of adenoid growth.

As has been suggested, where congenital narrowing of the bony nasal passages is present, and in cases of deflected septa, anterior and posterior hypertrophy of the turbinated bodies, guarded opinions should be rendered

to the patient in reference to complete relief and restoration of normal breathing, after this operation is performed.

Membranous Pharyngitis.—The treatment of pseudomembranous inflammation of the pharyngeal mucous membrane requires for its scientific basis a thorough bacteriologic study of the infecting microörganisms. The management of the disease of the Klebs-Loeffler variety is described in detail under the classification of diphtheria. This disease is simulated clinically by pseudomembranous formations that are attended by the presence of numerous streptococci, staphylococci, pneumococci, the fusiform bacillus, and the spirillum of Vincent. A vaccine may be prepared from a culture taken, or a stock preparation may be used in these cases with advantage, in addition to the local and constitutional treatment given. Antidiphtheritic serum in full dosage (5,000 units) should be given promptly if a question of doubt exists as to the possibility of diphtheria. These cases are contagious, especially among children, and the prophylaxis of a rigid quarantine with proper disinfection is worth the effort.

For destroying pseudomembrane, Loeffler's solution—which consists of toluol, 36 parts; absolute alcohol, 60 parts; and liquor ferri sesquichlorid, 4 parts—is most efficient. It should be applied in small quantity to the false membrane for about ten seconds. It is well to dry the area before the application, in order to avoid the danger of the solution flowing on to the healthy mucosa. The procedure is often attended by sharp pain for a while—extending to the ears.

Peroxid of hydrogen ranks second in efficiency. In children it may be used diluted with equal parts of limewater in the form of a throat douche, or irrigation. The large soft rubber bulb syringe is a most useful instrument for the purpose. The process should be repeated hourly through the day. The interval may be lengthened at night to afford time for sleep. When marked toxemia exists with exhaustion in this case, as well as in all diphtheritic cases, the irrigation must be performed with the least amount of exhaustion to the patient. It is better to accomplish this task with the head in the lateral position—the body remaining prostrate. Much harm may be done by disturbing the patient with nourishment, medication, and throat treatment at irregular intervals. An effort should be made (when the case is not too serious) to arrange a plan that will include every attention after a three-hour interval. The heart should be examined frequently for indications of circulatory distress. A specimen of urine should be examined every second day in order to detect early nephritis, which may also furnish much information of therapeutic value. An ice collar will minimize lymphatic absorption and add to the comfort and welfare of the patient.

Inasmuch as many pseudomembranous conditions are contagious—especially among children—a strict isolation and quarantine should be

enforced. A room with good sunlight and more than 2,000 cubic feet of air per person should be selected. All unnecessary furniture should be removed and such articles chosen for use in the sick room as may be readily disinfected. A moist alkaline atmosphere may be obtained by the boiling of a soda bicarbonate solution—a dram to the pint of water. Where it is impossible to use an electric heater, a tea kettle on a gas stove will answer the purpose. A piece of garden hose may be attached to the spout of the kettle, and steam sent in any direction. Croup kettles of several patterns may be obtained in the market, but they are undesirable and increase the labors of the nurse, besides the danger of fire imminent with an alcohol lamp. In the houses of the very poor the crude method of placing a very hot flat iron or very hot bricks in a pan containing a small quantity of alkaline water will serve the purpose very well in cases of involvement of the larynx. Ingenuity may be required in the management of the diet. Milk, eggs, and beef broth will furnish the basis of many palatable preparations. Ice cream and fruit juices are grateful.

Constitutional treatment in the form of tincture of the chlorid of iron, 1 part; and glycerin, 4 parts; 30 drops t. i. d. will prove of service. Whisky may be indicated at the onset of symptoms of exhaustion.

Vincent's Angina.—The differential diagnosis of this infection from follicular tonsillitis and diphtheria may be promptly determined by the microscopic examination of a specimen taken directly with the swab. Klebs-Loeffler bacilli may also be found by this method and many hours of early treatment gained in this way. The fusiform bacillus and the spirillum of Vincent succumb usually to the application of peroxid of hydrogen, strong nitrate of silver solution, trichloracetic acid, 50 per cent, Lugol's solution, 10 per cent chromic acid or methylene-blue. The latter preparation should be rubbed well into the affected area, which is usually the tonsils. The application of powdered arsphenamin to the infected zone is of great benefit.

Some epidemics show considerable mortality. An autogenous vaccine may prove beneficial, although these microörganisms are cultivated with difficulty.

Phlegmonous Pharyngitis.—This infective process is marked by superficial ulceration of the pharyngeal mucous membrane and is usually of streptococcic origin. Treatment is started with a free calomel and soda purge, followed by salines. Ice-bags to the neck and hot alkaline irrigation hourly are indicated. The ulcerated areas should be painted with nitrate of silver or argyrol, 20 per cent. Membranous formation may require light applications of Loeffler's solution or peroxid of hydrogen irrigation and antiseptic gargles. Orthoform insufflation may be used to relieve pain. In later stages with cellulitis of the neck, heat and free incision of suppurative areas may be necessary. General septic infection

should be combated with antistreptococcus serum or streptococcus vaccine. Large doses of quinin are administered with advantage.

The subcutaneous injection of 200 to 500 gm. of normal saline solution is an excellent supporting measure. The administration of strychnin and alcohol may be necessary.

When the acute symptoms subside, reconstructive tonics should be prescribed.

Neuroses of the Pharynx.—Neuroses of the pharynx, such as anesthesia, hyperesthesia, paresthesia, spasm of the pharyngeal muscles, sensations from foreign bodies, paralysis of the pharynx, include a considerable number of cases that call for differential diagnosis and treatment. They are particularly common in women about the climacteric.

Conditions of anesthesia are observed in epilepsy, hysteria, and general paralysis of the insane. Associated with progressive bulbar paralysis it becomes exceedingly serious. Neuroses are annoying to the patients and the physician.

In hay-fever peculiar sensations of burning, pricking, or itching may arise from the enlarged lymphoid follicles near the base of the tongue. These may be destroyed with the galvanocautery. These hyperesthetic conditions are greatly relieved in some patients by a sufficient dosage of the elixir of triple bromid. Excessive use of stimulants and tobacco may produce hyperesthesia.

Particular attention should be paid to investigation of the teeth and prophylactic measures along this line carried on.

An eroded surface may give rise to peculiar sensations of fishbones, pins, or spiculæ of bones which have wounded the mucous membrane. A careful X-ray of the region and inspection with Jackson's bronchoscopic spatula may give important information. Local applications of galvanism 10 to 15 m.a. with the laryngeal mirror may show a fishbone, toothpick, or other very small foreign body in a follicle of the tonsil, the pyriform sinus or at the base of the tongue.

Further investigation of early pharyngeal paralysis without a history of diphtheria may prove this to be one of the early symptoms of progressive bulbar paralysis. Some cases may be relieved by local anesthesia of the oropharynx and the passing of an esophageal bougie.

Hysterical paralysis of the pharyngeal muscles with the patient unable to swallow solid food in the presence of others may be relieved by suggestion, bromids, feeding at the time of treatment and galvanism.

TONSILLITIS

George E. Shambaugh

Acute Tonsillitis.—Acute inflammation of the faucial tonsils is extremely common. The clinical aspect of the condition varies widely in different cases. In its most usual form the tonsils present a more or less marked swelling associated with a congestion not only of the surface of the tonsil showing in the pharynx but also of the mucous membrane immediately surrounding the tonsil. Not infrequently the crypts of the tonsils become filled with plugs of desquamated epithelium, and in severe cases there may occur small areas of necrosis. This condition is known as lacunar or follicular tonsillitis. These forms of tonsillitis are easily recognized by the patient as well as by the physician. The clinical diagnosis of this condition from diphtheria is not always easily made, especially in the early stages. It is important, therefore, to make a bacterial examination as early as possible, since the value of antitoxin in diphtheria is much greater when given early.

There are a great many cases of acute tonsillitis which are not associated with any marked swelling of the tonsillar tissue. In these cases the presence of a characteristic epithelial plug in one or more of the tonsil crypts associated with the congestion over the tonsil makes a diagnosis very easy. In other cases, the absence of epithelial plugs or the failure to detect their presence, especially in the buried type of tonsil where the surface is hidden behind the anterior pillar of the fauces, obscures the diagnosis of acute tonsillitis. Patients will often deny having had attacks of acute tonsillitis but will admit having attacks of sore-throat. When such patients are examined during an attack of sore-throat, it will usually be found that they are suffering from an attack of acute tonsillitis. On the whole, there appears to be about as many cases of acute tonsillitis which are not recognized as such, as there are cases where the condition is diagnosed as tonsillitis. This applies as much to adults as to children. In the latter there is often no complaint even of sore-throat, and the condition is suspected because of the sudden rise of temperature, for which no other cause can be detected. Where the tonsils are small or of the buried type the local evidence of tonsillar disease is often not easily discerned. It is important to keep these facts clearly in mind especially because of the close relation which is now recognized to exist between acute, subacute or chronic infection of the faucial tonsils and the occurrence of many serious conditions, the result of systemic infection, which call for the disposal of the primary focus in the tonsil. Of the systemic conditions which owe their origin so frequently to attacks of acute tonsillitis should be mentioned especially acute endocarditis, acute nephritis,

and acute articular rheumatism. There are many other conditions, such as enlargement of the thyroid, acute iritis and appendicitis as well as gall-bladder infection and the various conditions which were formerly loosely denominated "rheumatism," which in the light of recent clinical studies are often accounted for plausibly as the result of systemic infection secondary to acute tonsillar disease. A systemic infection resulting from an acute attack of tonsillitis is very prone to be repeated by any subsequent recurrence of the tonsillar infection. It is extremely important, therefore, in the treatment of tonsils that these clinical facts should be kept clearly in mind. The treatment of acute tonsillitis includes very often more than the treatment of the acute attack. It should include a careful consideration of the question of prophylaxis against subsequent attacks of tonsillitis.

The treatment of acute tonsillitis is both general and local. The condition is usually quite contagious and it is important where feasible to enforce isolation. In view of the more serious complications, which so frequently follow acute tonsillitis, it is advisable to keep the patient in bed a few days until fever has subsided. Calomel should be given at night followed by a saline cathartic in the morning. Acetyl salicylic acid (aspirin), in 5-gr. doses, repeated every four hours assists a great deal in lowering the temperature and in relieving the associated headaches and muscle pains. Locally some simple gargle should be given. A teaspoonful of bicarbonate of soda in a tumblerful of warm water, or a normal salt solution, is usually all that is required. In the severe cases where the pain in the throat is great, the following gargle containing carbolic acid gives relief: carbolic acid, ½ dram; sulphocarbolate of zinc, 2 drams; water, 6 ounces. This is to be diluted from three to five times with warm water. When the breath is very offensive hydrogen peroxid diluted from three to five times with warm water may be used as a gargle. For local application to the tonsils, a great many agents have been recommended, including strong solutions of silver nitrate and of guaiacol. The discomfort associated with the application of these agents often outweighs any improvement which they may bring about. Argyrol in 10 per cent solution swabbed over the tonsil and by means of a curved cotton applicator, introduced behind the soft palate, is not unpleasant and accomplishes all that any antiseptic application can do. Iodin in the form of Mandel's solution applied to the surface of the tonsil may also be used—iodin 5 gr., potassium iodid 25 gr., glycerin 1 oz. When the discomfort from the infiltration of the tissues of the neck is very great, the application of a cold compress gives some relief. A cloth is wrung out of ice water and applied around the throat. Over this is placed a piece of oiled silk and about this compress is placed a suitable retaining bandage. The use of ice-bags may also increase the comfort of the patient.

Formation of an abscess in the tonsil (quinsy sore-throat) or of an abscess in the tissue about the tonsil (peritonsillar abscess) requires in addition to the treatment for acute tonsillitis the surgical opening of the abscess. The formation of an abscess in the tonsil is recognized by the increased swelling of the tonsil, crowding it toward the median line, and by the presence usually of edema of the anterior pillar and uvula. The abscess usually points on the free surface of the tonsil. A peritonsillar abscess forms usually about the apex of the tonsil between the layers of the soft palate. It is especially apt to occur in the type of tonsil where the upper lobe is deeply imbedded. The infiltration is more above the tonsil and causes a diffuse bulging of the soft palate towards the median line. A serious complication of phlegmon of the tonsils is the development of an edematous infiltration of the lateral bands of the pharynx just back of the tonsils. This edema tends to extend downward and may produce edema of the glottis, necessitating intubation or tracheotomy.

The incision for opening an abscess in the tonsil is made toward the base of the tonsil. The point of the bistoury should not be directed laterally but straight back. The incision for a peritonsillar abscess is made through the soft palate above the tonsil. It is often necessary to plunge the instrument from one to two inches into the swelling before the abscess is reached. If care is taken to direct the point of the instrument straight back and not to the side, there need be no fear of causing injury by introducing the instrument too far. When the abscess is entered, pus will at once appear along the sides of the knife. On withdrawing the instrument the size of the opening should be increased by cutting parallel with the free border of the soft palate. In spite of a large opening, it sometimes becomes necessary after a few days to introduce a blunt probe and reopen the passage. A general anesthetic is contra-indicated in these cases, and the local application of cocain is of little assistance. It is important, therefore, that the instrument used should have a fine point and a keen edge, and that the operation should be done as quickly as possible. The method sometimes recommended of making a small opening through the mucous membrane, through which a blunt instrument is plunged deep into the tissue, increases the suffering very greatly and has no advantage over the quicker and much less painful method of using a sharp instrument.

The treatment of tonsils which have been the seat of acute infection has become a much more important matter since the recognition of the frequency with which systemic infection occurs as the sequel of tonsillitis. Formerly, the situation was met by an attempt to remove part of the tonsil with a tonsillotome, provided the tonsils were large enough to be secured by this instrument. The operation was restricted almost exclusively to children. In adults the type of tonsil that could be operated on successfully by the method in vogue was rather the exception. Various

methods were devised to treat such tonsils in adults. Fragments of the tonsils were removed with biting forceps, and the operation repeated several times, until a large part of the parenchyma of the tonsil had been removed. In other cases the surface of the tonsil was repeatedly cauterized with an electric point. In some cases the crypts were torn open with blunt or sharp instruments, followed by the introduction of an electric point into the enlarged pocket in an effort to obliterate the crypts.

In more recent years all these methods have given way to the operation of enucleation of the tonsils. The reason for the resort to a more radical operation has been twofold. In the first place was the failure in many cases to prevent recurrence of the attacks of acute tonsillitis by the older methods of operating as well as the better appreciation of the danger in subsequent attacks in cases where there has once been systemic infection such as arthritis, endocarditis or nephritis. In the second place it became apparent that in many cases where the tonsils had been partially removed or where the surface and crypts had been cauterized, even though there might be no subsequent attacks of tonsillitis, there often persisted a state of chronic infection of the tonsils which became a dangerous focus capable of causing systemic infection resulting in such serious conditions as chronic neuritis, cardiovascular degenerations, chronic arthritis and chronic nephritis. To prevent not only the possibility of a recurrence of acute tonsillitis, but also the possibility of persistent chronic latent foci of infection in the tonsil stubs, enucleation of the tonsil has been resorted to.

A single attack of acute tonsillitis when not associated with systemic infection hardly warrants the advice to have the tonsils removed, unless this single attack results in unmistakable evidence of persisting infection in the tonsils (see Chronic Tonsillitis, following). Whenever, on the other hand, there develops a distinct tendency to recurring attacks of acute tonsillitis, or when a single attack of tonsillitis has resulted in such a serious systemic infection as acute endocarditis, nephritis or articular rheumatism, the advice should be given to have the tonsils removed, that is, enucleated.

Chronic Tonsillitis.—A great deal of progress has been made in recent years in the recognition of chronically infected faucial tonsils. The internist has called attention to the frequency with which chronic, often latent, foci of infection are responsible for the persistence of systemic infections resulting in chronic neuritis, chronic arthritis, cardiovascular degenerations and nephritis, as well as the probable etiological relation of these foci with such conditions as enlargement of the thyroid, gall-bladder infections, gastric and duodenal ulcers, and appendicitis. The result is that the specialist in diseases of the throat has been led to examine the tonsils much more closely than heretofore, and many cases of chronic infection of the tonsils are detected which were previously overlooked.

Formerly, about the only type of chronically infected faucial tonsils which was recognized and given serious consideration was the type where the tonsils became chronically enlarged, especially when they showed a persistent state of congestion. The removal of such tonsils, particularly in children, has long been practiced, and it has long been recognized that the striking improvement in general health which so frequently follows this operation could be plausibly accounted for only on the assumption that the infected tonsils were producing a persistent though mild systemic infection.

In gathering the evidence which should place suspicion on the tonsils as a possible focus for infection, the history of recurring attacks of acute tonsillitis should have first consideration. Tonsils which are known to be the seat of such recurring attacks should always be suspected of harboring chronic foci of infection, exactly as we would condemn an appendix which is the seat of recurring attacks of acute inflammation. As pointed out in the previous section on Acute Tonsillitis, many cases of acute tonsillar disease pass unrecognized as such by the patient. The local symptoms are looked upon as the result of a sore-throat but not of a tonsillar infection. The history of recurring sore-throat even when the patient asserts that there have been no attacks of tonsillitis should always be regarded with suspicion. The history of an attack of quinsy or of a peritonsillar abscess is always suspicious since these conditions frequently leave persistent latent foci of infection in the depths of the tonsil.

An examination of the tonsil will disclose distinct evidence of chronic infection in a great many cases even when there is nothing in the history of the throat symptoms that would throw suspicion on these structures. Tonsils which are the seat of chronic infection are very often enlarged. The exposed surface of the tonsil as well as the neighboring tissue, especially over the anterior pillars, is often more or less congested. In many cases the crypts are enlarged and contain foul-smelling cheesy plugs. Pressure with a blunt instrument along the outer boundary of the tonsil will often express large masses of epithelial débris from the deeper lacunæ. and especially from the more embedded upper lobe of the tonsil. Occasionally by pressure in this way, pus can be expressed from a chronic abscess in the depths of the tonsil. The presence of cheesy deposits or even of pus is not restricted to the tonsils which are chronically enlarged but are as apt to be found in tonsils which through the hypertrophy of the connective tissue stroma have undergone a shrinking with elimination of a large part of the parenchyma. A particularly suspicious type is the tonsil which is deeply embedded between the layers of the soft palate, with only a small surface exposed to view even after the anterior pillar has been pulled aside. Tonsils of this type are often much enlarged and yet nothing is seen of them by the casual inspection of the pharynx. It is now a well-recognized clinical fact that a tonsil which has been

previously operated on and partially removed, or where the surface has been scarred over by the use of the cautery, is especially likely to retain chronic foci of infection capable of causing systemic disease. It is not uncommon when operating on tonsils to discover pockets of pus the presence of which was not disclosed by a careful previous examination.

These clinical facts, which have been observed over and over again by the men working on the tonsils, taken in connection with the rôle played by chronic foci of infection in the etiology of systemic disease, have brought about a decided change in our treatment of chronically infected tonsils. Local treatment of tonsils, the seat of chronic infection, has not been found to be of any very positive assistance in most cases. The complete enucleation of the tonsil is the one treatment which we have of making sure that the infection has been eliminated. This does not mean, however, the indiscriminate removal of tonsils even when there exists some of the evidence just discussed that the tonsils are not entirely normal. The decision to remove the tonsils depends on two factors. The first is the character of the evidence of infection discovered in examining the tonsils. The second is the presence as well as the character of a systemic infection, which the tonsils may be suspected of causing. Tonsils which are the seat of recurring attacks of inflammation should be removed. This applies as well to small as to large tonsils and as well to adults as to children. Tonsils which are decidedly enlarged, especially when the crypts contain foul-smelling, cheesy plugs or where the persistence of a distinct congestion indicates the persistence of infection, should be removed even though there is no evidence of acute attacks of tonsillitis. Tonsils from which pus can be expressed should be removed even though they are causing no local symptoms, and even though no evidence of systemic infection is recognized. A single attack of tonsillitis, even though the tonsils have not been left enlarged, if complicated by a serious systemic infection such as acute rheumatism, endocarditis or nephritis, calls for enucleation of the tonsils as a prophylactic measure against the recurrence of the systemic trouble. Tonsils which are not the seat of recurring acute inflammation, which are not distinctly enlarged, and from which pus cannot be expressed but which do exhibit some of the evidence discussed above of chronic infection, such as the presence of cheesy deposits in the lacunæ, hardly call for removal unless the patient is suffering from a serious systemic infection, for which no other probable focus can be discovered. On the other hand, I have several times removed tonsils when the internist has advised the operation because the patient was suffering from a serious systemic infection for which no probable focus could be discovered, when there was no history of acute tonsillitis and where I had not been able to discover any local evidence of tonsillar infection, and I have been surprised at disclosing at the time of operation an abscess deep in the tonsil. The conclusion forced upon one by such

experiences is that when a patient is suffering from a serious systemic infection which is known to be of focal origin, and when a thorough-going examination by a competent internist fails to discover any probable focus, one is justified in removing the tonsils, especially since it is known that they are the most frequent seat of such infection.

It is evident from this discussion of the treatment of chronically infected faucial tonsils that many cases can be handled intelligently only through the coöperation of the throat specialist and the internist. This is especially the case where systemic infection exists.

The operation for enucleation of the tonsils (tonsillectomy) has now been generally adopted throughout the world in place of the operation formerly practiced of a partial removal (tonsillotomy). The operation of enucleation was a logical result of the discovery of the important rôle played by chronic tonsil infection in causing systemic disease, and the recognition that a partially removed tonsil often harbored chronic foci of infection which kept up the systemic trouble. The importance of focal infection in the etiology of systemic disease was largely worked out in this country and the operation for the enucleation of the tonsils came also as a contribution from America. It had been practiced here for a number of years before the operation was taken up abroad.

It would hardly be proper in this connection not to call attention to the development in recent years of a more or less general tendency toward indiscriminate removal of the tonsils. This has been the direct result of the practice of teaching the technic of operations in this special field to interns in general hospitals and to general practitioners who come to our clinics long enough to learn the technic of the operations but who are not willing to spend the time necessary for acquiring a proper appreciation of the indications. It is always much easier to teach one the technic of such operations than to instill a proper understanding of the indications. The indiscriminate removal of tonsils in cases where a complete examination would disclose no local or general condition which should lead one to suspect these structures as the source of trouble is, of course, to be deprecated. Much of the existing unnecessary, indiscriminate removal of the tonsils could be avoided through a proper coöperation between the throat specialist and the internist. The throat specialist who attempts to decide on the removal of tonsils in cases of systemic infection is very likely to remove these structures where a careful examination by the internist could determine that some other much more probable focus exists, or that the general symptoms complained of are not the result at all of focal infection.

On the other hand, the discriminating diagnosis of those conditions found in the tonsils which constitute a proper indication for tonsil removal, especially in cases of chronic tonsillitis, can be properly made only by those who are specializing in this field of work. It is a common

error to refer to the cheesy concretions so commonly found in the tonsils of adults as accumulations of pus. The two conditions have a widely different clinical significance, for whereas pus in the tonsil is always recognized as a menace justifying the removal of the tonsils, the presence of cheesy concretions can often be overlooked, especially where there is no history of recurring attacks of tonsillitis and no systemic infection that is unaccounted for by foci of infection elsewhere.

One encounters many cases, particularly in adults, where there is no suspicion of systemic infection and where the local findings in the tonsil hardly justify their removal, and yet where the lacunæ contain cheesy plugs, which cause more or less annoyance to the patient especially by giving an offensive odor to the breath. In such cases, one is often justified in attempting to relieve the trouble by repeatedly slitting open the offending lacunæ, by syringing out the cheesy plugs and by the use of the electric cautery. There are occasional cases, too, where both because of the presence of a systemic infection and from the local findings in the tonsils one would ordinarily be justified in removing these structures, but where because of a high blood-pressure and a slow coagulation time the risk of a dangerous bleeding might deter one from the radical operation. In such cases one may try the safer though usually much less effective measures outlined above for getting rid of the tonsillar infection.

The enucleation of the faucial tonsils is not a minor surgical procedure, as was the older method of amputation of part of the tonsil. Enucleation, particularly in adults, where the tonsils have become adherent, as is frequently the case after a peritonsillar abscess, is an operation fully as difficult and because of the risk of subsequent hemorrhage fully as dangerous as an operation on the appendix. The failure to appreciate this fact has been responsible for not a few cases of fatal hemorrhage, not to speak of permanent injuries to the throat when the operation has been undertaken by the practitioner inexperienced in the technic of this sort of work.

In children the operation can only be done under a general anesthesia. Ether is found to be the best agent for the work. Chloroform is contraindicated, as it has been shown to be particularly dangerous in cases of marked hypertrophy of the lymphatic structures of the throat. Nitrous oxid, because of the increased bleeding and the necessity for haste in completing the operation, is not so suitable in the hands of most operators as is ether. In young children, moreover, it has been found to be decidedly more dangerous than ether. Such anesthetics as ethyl chlorid and ethyl bromid have been given up since they have been found to be practically as dangerous as chloroform. The handling of the anesthesia is more important than in most operations, since it is more difficult to give an anesthetic properly for a tonsillar operation. In the first place, unless the anesthesia is deep enough, the operator is working at a disadvantage

because of the patient's gagging, and, in the second place, an anesthesia pushed too far brings with it unusual dangers in operations on the tonsils, especially from the inhalation of the blood. For these reasons the advantage of having a trained anesthetist assist in tonsillar operations is becoming more and more recognized.

The position of the patient during operation is important. Some operate with the patient sitting upright, some with the head dropped back over the end of the table and others with the patient lying on the back. Some apply specially devised suction apparatus for keeping the field of operation free from blood, while others operate with the throat full of blood.

An operator may become accustomed to any of these methods of operation and does his work best when following the method to which he has become accustomed. All things considered, it is better for the patient to be in a reclining position while taking a general anesthetic. In the same way it is evident that, other things being equal, it is better for the throat to be free from blood during the anesthesia. The occurrence of abscesses in the lungs after tonsil operations performed under general anesthesia, is probably the result of inhalation of blood with infected material from the tonsils.[1] We have found that having the patient lie on the side so that the blood will flow naturally from the mouth is the simplest way of overcoming the annoyance to the operator from the bleeding as well as the danger to the patient of inhaling the blood. The operator sits on a chair beside the patient and the lower tonsil is removed first. All bleeding should be checked before the patient is allowed to come out from the anesthesia.

The large number of different instruments that have been devised in recent years for this work speaks eloquently for the difficulties that have been encountered by operators in undertaking the enucleation of the tonsil. No one method of operation is best suited for all cases. In children, the usual type of enlarged tonsil can as a rule be readily shelled out from its bed by forcing the tonsil by means of the finger through the opening of an old-fashioned Mackenzie tonsillotome. In other cases where the tonsils require removal but where they are not enlarged, and especially where they are of the embedded type, the operation is often accomplished with the least traumatism by seizing each tonsil with the forceps, and drawing it toward the median line. The upper pole is then loosened by cutting with a sharp scalpel the mucous membrane along the line of its attachment to the tonsil. With this accomplished, the tonsil can be pulled through the loop of a stiff wire snare, and cut off slowly enough to prevent bleeding.

[1] The editor feels that this point cannot be overstressed. There are far too many lung abscesses following tonsillectomy and almost all of them can be avoided by a proper technic.—Editor.

The operation for enucleation of the tonsils in adults is quite a different procedure, since in most cases it is best to do the operation without employing a general anesthetic. With the use of a local anesthetic the risk to the patient is distinctly less than when ether is used. The bleeding is less, and is more readily controlled with the patient conscious and in the upright position. On the whole the discomfort to the patient with a properly administered local anesthetic is very much less than when ether is employed. Nitrous oxid as an anesthetic is not especially suitable to these cases, first, because, with the usual type of tonsils in adults where they are not greatly enlarged, the patient experiences no pain, provided the operator has had sufficient experience in the technic of local anesthesia. In the second place, the cases where the local anesthesia fails to give complete insensibility to pain are the cases where the tonsils are greatly enlarged, and especially where they are adherent through inflammatory reaction. In these types of cases the time required to do properly the necessary dissection is not sufficient when gas anesthesia is used.

In nervous individuals it is often a decided advantage to administer hypodermically morphin $\frac{1}{6}$ to $\frac{1}{4}$ gr. with atropin before the patient is taken up to the operating room. The operation should not be undertaken soon after a meal, as the annoyance from gagging is thereby greatly increased. Local anesthesia is begun by applying with a cotton swab around the attachment of the tonsil 5 per cent cocain made up in an adrenalin solution. When the patient begins to experience the local effect of the cocain by the development of a sensation of fullness in the throat, a solution of novocain, $\frac{1}{2}$ of 1 per cent, should be injected about the tonsil with a suitable curved needle. A few drops are injected beneath the mucous membrane at one or two points along the posterior pillar. As much as $\frac{1}{2}$ dram of the novocain may be injected into the lower pole of the tonsil. The most important part of the local anesthetic is the injection of a sufficiently large quantity of the novocain into the base of the tonsil. The proper point for making the injection can usually be determined by locating the outline of the tonsil through the soft palate. The needle is then pushed through the anterior surface of the soft palate deep into the tissue. If the point of the needle has failed to penetrate under the tonsil the injecting fluid will escape through the lacunæ. In cases where the embedded velar lobe of the tonsil is very large or where, as the result of peritonsillar inflammation, the normal demarcation between the base of the tonsil and the neighboring tissue has been obliterated, it may be quite difficult to get the solution injected so that it does not escape through the tonsil lacunæ.

With the local anesthesia completed the patient is directed to hold the tongue depressor in place while the operator seizes the left tonsil with a suitable forceps held in his left hand. The tonsil is drawn down-

ward and toward the median line. With a straight sharp scalpel held in the right hand, the operator incises the attachment of the mucous membrane along the anterior upper part of the tonsil. Then without detaching the forceps this instrument is seized quickly with the right hand and with the scalpel in the left hand the mucous membrane is incised along its attachment just in front of the posterior pillar. In the same way, the right tonsil is dissected from its attachment, especially around the upper part. Only after both tonsils are dissected free in this way is the effort made to pull the first tonsil through the loop of the stiff wire snare. By tightening the snare slowly, the tonsil can be removed as a rule with very little bleeding.

The control of subsequent bleeding may often be much more difficult than the operation itself. In case the primary bleeding does not stop promptly and completely, the bleeding point must be searched for at once, and seized with a curved artery forceps. The usual point of bleeding is from the tonsillar artery near the middle of the tonsil fossa. Occasionally the bleeding point is in the upper part of the tonsil fossa or near the lower pole. The artery forceps may be left in place for from fifteen to twenty minutes after the patient has been taken from the operating room. Very troublesome is the bleeding which trickles down the esophagus without the patient knowing it. The nausea associated with the accumulation of blood in the stomach increases greatly the anxiety of the patient. When a secondary bleeding occurs in a nervous patient it is usually an advantage to administer morphin hypodermically $\frac{1}{6}$ to $\frac{1}{4}$ gr. with atropin. This alone frequently results in a prompt cessation of the bleeding. The simplest mechanical means of stopping the bleeding is by pressing a ball of cotton soaked in peroxid into the tonsil fossa. The excess of peroxid should be squeezed out of the cotton and the pressure kept up as long as the patient will permit. In case this does not suffice to stop the bleeding, it is usually advisable to proceed at once to search for the bleeding point. This is done by first wiping out all the clots from the fossa, then with reflected light the bleeding point is looked for and, when found, seized with the curved artery forceps.

The patient is better off sitting up in bed with a back rest for a few hours after the operation, and is often made more comfortable by having ice-bags around the throat. A simple gargle every three or four hours begun the day after the operation and kept up for about a week is the only after treatment that is called for. A teaspoonful of bicarbonate of soda in a tumblerful of warm water is as useful as any gargle. The unpleasant taste in the mouth, which persists for several days after the operation, may be relieved somewhat by the occasional use of a gargle of peroxid diluted in water. During the first few days after the removal of the tonsil, usually not over one week, there is always considerable discomfort in swallowing either liquids or solid food. Much of this discom-

fort can be avoided by administering to the patient 10 gr. of aspirin twenty minutes before eating.

In recent years efforts have been made to avoid the operation of removal of tonsils by reducing these structures through the use of X-ray or radium. To what extent this may prove successful has not as yet been determined. The method, however, is not without its objection. The effect on the neighboring glands has been noted, where, as the result of atrophy, there is a persistent dryness due to the lack of normal secretions. While it is a well-recognized fact that radium is capable of reducing lymphoid hypertrophies, it is not apparent that the persistence of infection in tonsils shrunken by this method is eliminated any more than is the case where, as the result of the hypertrophy of the connective tissue stroma in chronic tonsil infection, there results a marked shrinking of the tonsil with absorbtion of the lymphoid tissues. Tonsils shrunken in this way have been found to harbor persistent foci of infection as frequently as does the well-known hypertrophied tonsil. Clinical evidence seems to indicate that while the use of the X-ray or radium is capable of bringing about a decided shrinking of the hypertrophied tonsil it is not apparent that there results an elimination of the dangerous chronic foci of infection. It would appear, therefore, that, where the indication for the removal of the tonsil is the presence of a serious systemic infection, the operation of enucleation of these structures is the proper procedure. The use of radium seems more suitable for the removal of those lymphoid hypertrophies in the lateral bands of the pharynx which occasionally persist and sometimes only appear after the tonsils have been removed.

CHAPTER XXIX

DISEASES OF THE ESOPHAGUS

BERTRAM W. SIPPY

The esophagus begins at a point behind the lower border of the cricoid cartilage on a level with the sixth cervical vertebra, and joins the stomach about three-fourths inch after passing through the diaphragm. The lower end of the esophagus is on a level with the spine of the twelfth dorsal vertebra. In a normal adult the upper end of the esophagus is about six inches from the incisor teeth. Measuring from the incisor teeth it is about ten inches to the bifurcation of the trachea, eleven inches to the point where the left bronchus crosses in front of the esophagus, and sixteen inches to the lower end of the esophagus. The esophagus serves the purpose of conveying food and drink from the pharynx to the stomach. Corresponding to its simple function, its anatomical structure is simple, and disorders of the esophagus other than those associated with conditions causing esophageal obstruction are relatively rare.

ESOPHAGEAL STENOSIS

Stenosis is by far the most important disorder of the esophagus. The treatment of esophageal obstruction is governed by the cause, location, and degree of stenosis. In all cases early diagnosis is of great importance. Although in a given case there should be no difficulty in determining that stenosis of the esophagus is present, experience shows that the condition is frequently overlooked or mistaken for a gastric or some other disorder. The symptoms vary with the cause and location of the stenosis. As a rule, the patient first notices that deglutition is uncomfortable. A choking sensation or a sense of fullness behind the sternum is experienced. He is compelled to eat slowly, and, as the obstruction increases, regurgitation of food is likely to occur either during the meal or shortly afterward. Nausea is usually absent. Pain may be a prominent feature or may be entirely absent.

Direct observation of the patient during the act of swallowing is of

great value in diagnosis. Many serious mistakes would be avoided by carefully observing the patient eat and drink when difficulty or pain in swallowing or when vomiting at mealtime is a feature in the symptomatology. Suspecting that stenosis is present, thoracic aneurysm should be excluded, and then, if no other contra-indication exists, an attempt should be made to pass a soft rubber stomach tube. If successful the degree of stenosis is slight, and, if any exists, it may be accurately located by means of an ordinary esophageal bougie armed with graduated olive bulbs. A medium-sized bulb should be used first. If this meets with obstruction the smallest-sized bulb may be used next. Great caution should be exercised regarding the use of force.

To determine the nature of esophageal obstruction is often difficult. Carcinoma is by far the most common cause in adults. In order to avoid serious error, however, in every case of esophageal stenosis all other causes should be carefully excluded before it is assumed that carcinoma is present.

The following conditions may cause esophageal stenosis: anatomical disease either of the esophagus or adjacent structures, spasmodic contraction of its muscular fibers, and the impaction of foreign bodies.

Extra-esophageal disease causing stenosis is relatively rare, but compression from aneurysm, mediastinal growths, extra-esophageal cicatrix, a distended diverticulum of the esophagus, pericardial exudate, and disease of the vertebræ must always be considered as possible causes of esophageal compression, resulting in obstruction. Thyroid and thymus tumors, enlarged cervical glands, and retropharyngeal growths may also produce stenosis.

Intra-esophageal conditions causing stenosis may be from cicatricial narrowing, tumor (chiefly cancer), spasmodic contraction of the esophageal muscle (chiefly cardiospasm), diverticula, and the impaction of foreign bodies.

Cicatricial Stenosis of the Esophagus

Next in frequency to carcinoma, cicatricial contraction is the most common cause of esophageal stenosis. From a therapeutic standpoint it takes first rank, because the treatment of cicatricial stenosis should be reasonably satisfactory in all cases. The most frequent cause of cicatricial stenosis of the esophagus is the swallowing of caustic acids, alkalis, and other corrosive substances. More rarely cicatricial stenosis results from the healing of ulcers due to the impaction of foreign bodies, the peptic action of the gastric juice, and ulceration of the esophagus that occurs during the course of typhoid fever.

Treatment.—During the first week or ten days subsequent to severe corrosion of the esophagus, as from caustic acids or alkalis, no attempt

should be made to pass dilating bougies. After the intensity of the inflammation has subsided, bougies should be passed at least once or twice each week until the maximum-sized lumen is obtained. The passage of the bougie is facilitated by directing the patient to drink half an ounce of olive oil just preceding its use. The maximum dilatation should be maintained by using the bougie every few weeks, perhaps for years, as experience with the individual case may require. Usually patients with cicatricial narrowing of the esophagus do not apply for treatment until the scar tissue is old and firm. In many cases real obstruction does not occur until years after the injury to the esophagus. If the stricture is not long and tortuous, ordinary olive-tipped esophageal bougies may be passed, beginning with a small-sized bulb that may go through the stricture without the use of dangerous force. The opening should be cautiously enlarged by using bulbs of gradually increasing size. The rapidity with which dilatation should be accomplished is influenced by the resulting inflammatory reaction, fever, pain, hemorrhage, and the length and firmness of the cicatricial narrowing.

It is impossible to dilate successfully a long, narrow, and tortuous stricture with an ordinary esophageal bougie of the whalebone or steel rod type. The whalebone or steel rod is too inflexible to follow the tortuosity of the canal. In such cases the conical-tipped flexible linen bougie with a gradually increasing diameter is used; but great caution must be exercised, otherwise a false passage may be made. The small conical tip of the flexible bougie is trusted to enter the opening or channel leading into the stricture, and in many cases to follow the windings of a tortuous and, at times, a sloughing canal, and thus guide the thicker dilating portion of the instrument safely through the stricture. It is truly remarkable how many times such bougies may be used without serious accident. Experience has abundantly demonstrated, however, that the point does not always follow the canal. Many deaths have resulted from perforation of the esophageal wall by the use of such bougies.

It is obvious that there must be great danger in forcing any form of unguided bougie through a strictured area of the esophagus. The numerous operations that have been devised whereby artificial channels, independent of the esophagus, have been constructed to serve as a substitute for the strictured esophagus, emphasize the danger and inefficiency of the dilating whalebone and flexible linen types of esophageal bougie in common use to-day.

To obviate the danger and increase the efficiency of the bougie method of treating organic esophageal strictures, the writer has devised an esophageal dilator by means of which, if properly used, cicatricial stenosis of the esophagus may be safely and permanently relieved without great discomfort or inconvenience to the patient. Because of the very greatly increased safety and efficiency of this method of dilating esophageal stric-

tures, the writer makes use of this method in all cases of organic stricture of the esophagus that admit of the use of any dilating instrument. The advantages are particularly striking when dealing with tight and tortuous strictures, whether due to cicatricial contraction or carcinoma. The principle of using the silk thread as a guide is utilized in the following manner:

A foot or more of a spool of ordinary silk twist, such as Belden or Corticelli, size D, is placed in a small capsule or wadded up in a piece of chocolate candy and swallowed. After about an hour the spool is slowly unwound, so that 3 or 4 yards is swallowed during the first eight or ten hours. Subsequently from 1 to 3 yards may be swallowed each day. The taking of food and water facilitates the passage of the thread into the stomach. If the stricture is extremely tight only a small amount of water should be swallowed at one time. If the esophagus is overfilled, its contents, including the thread, are likely to be regurgitated. A small twisted silk thread will eventually go through any stricture that will permit the passage of even a small quantity of water. After the silk reaches the stomach, the normal peristalsis carries it onward. Usually at the end of twenty-four hours the thread that was first swallowed becomes deeply anchored in the intestine. It later passes out through the rectum. The thread is ready for use as soon as it is determined that it is securely anchored by pulling back on the end attached to the spool. The dilator (Fig. 1) consists of

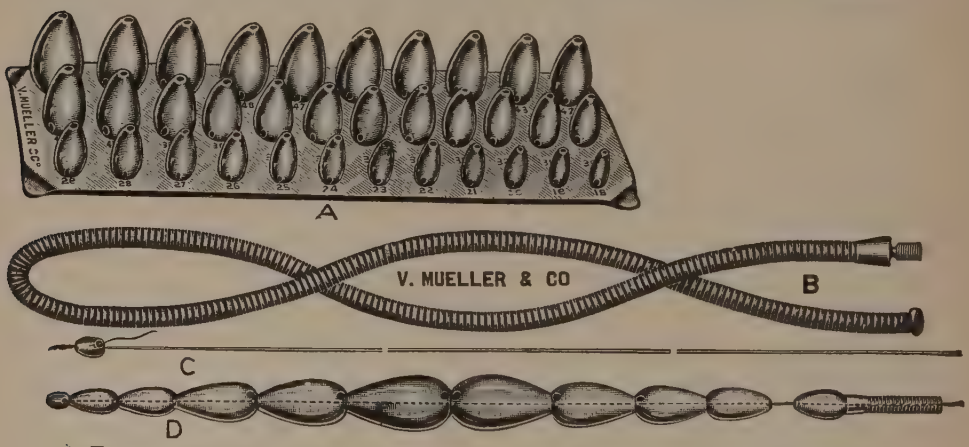

Fig. 1.—Flexible Esophageal Dilator and Piano-wire Guide. (Sippy.)

a series of graduated conical metal bulbs (A) that may be screwed on to a very flexible spiral introducer (B) 20 inches long, made of piano wire, size No. 8. Each conical bulb is provided with a central canal that is continuous with the lumen of the spiral introducer when the bulb is adjusted. This canal is large enough to glide readily over the piano wire guide (D). The guide is 4 feet long and made of piano wire, size

No. 20. A small perforated metal bulb, size No. 10, French scale, is firmly secured to one end of the wire by screw and solder. For a distance of 8 inches adjacent to the bulb the wire is reduced in size to increase its flexibility. Wires in constant use may crystallize near the bulbous point and should be discarded after prolonged use, particularly if signs of rust appear. The silk thread protruding from the mouth is first drawn back from the esophagus until it is moderately taut. The thread is then passed through the perforated bulb on the end of the piano wire guide. Holding the silk thread taut with the hand, the wire guide is introduced into the esophagus. The bulb follows the course of the thread and carries the wire safely through the stricture into the stomach. The lower end of the wire should be passed at least 4 or 5 inches beyond the lower end of the esophagus. If the thread is held firmly no harm can result even if the wire enters the pylorus. The wire is easily held in position and serves as a firm guide for the conical bulbs used in dilating the stricture.

The diameter of the stricture is next determined by attaching a conical bulb to the spiral introducer, and passing the bulb and introducer over the wire and through the stricture. Beginning with a small-sized bulb, larger ones are substituted until one is found that passes through the strictured area snugly, without force. A bulb slightly larger in diameter is selected for the first dilatation. The following procedure is advised: By means of the silk, the wire guide is introduced until its bulbous point has reached the pylorus. A bulb several sizes smaller than the diameter of the stricture is then threaded point downward over the guide. From one to three bulbs, each slightly larger than the one preceding, are then threaded, to be followed by the dilating bulb. A similar cone of two or three bulbs is next threaded with points directed upward. The spiral introducer with a small-sized bulb attached is next threaded on the wire. The operator then holds the end of the wire guide firmly in one hand. The detached bulbs sliding on the wire are then pushed down through the stricture by the spiral introducer. The first bulb, being several sizes smaller than the diameter of the stricture, enters without friction, opening the way for the slightly larger bulb immediately behind it. The next bulb, being still larger, prepares the way for the dilating bulb, which enters the stricture in such a way as to exert an almost purely lateral or dilating pressure. All the bulbs are pushed through the stricture and into the stomach. The bulbs are drawn back through the stricture by means of the wire guide. As the guide is withdrawn the tiny bulbous point securely fastened at the lower end comes in contact with the lowest conical bulb, which forces all the other bulbs backward through the stricture. The small bulb at the end of the introducer opens the way for the conical bulbs threaded with points upward. The stricture is thus gradually opened from below, so that the dilating bulb enters

the stricture both from above and below with the least possible traumatism to its walls. The pressure exerted in forcing the bougie is applied in such a way as to act almost entirely as a dilating force. The operator is enabled to judge with a great degree of accuracy the readiness with which the tissue of the stricture yields. Thus friability of tissue with perhaps increased dangers, or firm connective tissue requiring more force, may be suggested. If thought best, one or more larger-sized dilating bulbs may be used in the same manner at each treatment. The rapidity with which a stricture may be safely dilated is influenced by the character of the stricture, its length, the dilatability and friability of its tissue, and such factors as pain, hemorrhage, inflammatory reaction, and other conditions peculiar to the individual case.

An extra set of smaller bulbs (E, Fig. 2), a finer wire guide with a tiny bulbous point and a spiral introducer made correspondingly smaller in diameter, are required for the treatment of strictures too tight to admit the No. 10 (French scale) bulbous point on the wire guide of the larger set.

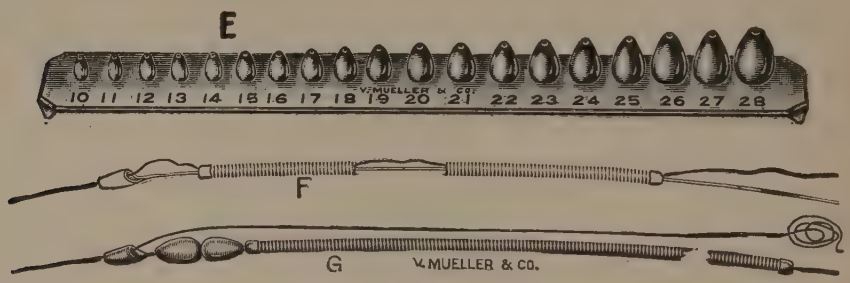

Fig. 2.—Esophageal Dilator for Use in Dilating Extremely Narrow and Tortuous Strictures. (Sippy.)

In attempting to dilate tight, long and tortuous strictures the channel may be so narrow and irregular that the bulbous point on even the finest wire guide becomes arrested upon attempting to introduce it, using the silk thread as a guide as described. In such cases the wire guide may be introduced as follows: First pass the thread through the lateral canal of the tiny bulb on the end of the small wire guide; then pass both thread and wire through the small-sized spiral introducer (F, Fig. 2). Pulling the thread guide taut, the spiral stiffened by the taut thread may be pushed through the narrow tortuous stricture, carrying the bulbous point of the fine wire before it as far as the pylorus. Grasping the protruding end of the fine wire guide firmly in one hand, with the other the spiral introducer is withdrawn by sliding it backward along the wire guide in such manner as to leave the fine wire guide in position. The finest bulbs of the small set are then threaded on the fine wire guide (G, Fig. 2), according to previous directions, and pushed down through the stricture by the

small-sized spiral introducer. It should rarely be necessary to perform gastrostomy for the purpose of feeding a patient afflicted with cicatricial stenosis of the esophagus, provided the opening through the stricture is large enough to allow even a small quantity of water to pass. Surgical procedures devised for the construction of substitute channels for the esophagus strictured by cicatrix should virtually never be necessary or justified. A cicatrized esophagus will virtually always permit water to trickle through into the stomach. With rare exceptions a silk thread will eventually find its way through and become anchored in the intestine. Using the silk thread as a guide, an appropriate-sized flexible wire guide may be introduced through the stricture and as far as the pylorus. Cicatricial strictures of the esophagus invariably yield to a proper dilating force. Appropriate-sized bulbs introduced on the wire and pushed through as described enable one to enlarge the lumen of the esophagus to the desired size. Cicatricial narrowing of extreme degree involving the entire length of the esophagus may be dilated sufficiently to enable the patient to eat ordinary food without embarrassment.

In many instances, the writer has thus reconstructed the esophagus several years after it had been deemed necessary to perform gastrostomy to prevent starvation. In such cases within a short time after the dilatation was begun the gastrostomy opening was allowed to close. In dilating tight, long and tortuous strictures, as soon as the lumen of the esophagus is enlarged sufficiently to allow an adequate intake of liquid food, one should proceed slowly with further dilatations. The subsequent treatments should range from four days to two or more weeks apart, depending on the individual case. As a rule it is unwise to enlarge the stricture more than 1 or 2 mm. at a given stretching. Not infrequently one may well be content at a given treatment to maintain the channel without using a larger dilating bulb than was used at the previous stretching. The more slowly the strictured esophagus is dilated, the less the traumatism and resulting reactionary inflammation and connective tissue growth.

In adults it is seldom desirable to dilate finally with bulbs larger than 40 or 42 mm. in circumference. In children the lumen of the strictured esophagus may be stretched proportionate to the size of the child. In all cases, if care and skill are exercised, stretching sufficient to allow the child to eat ordinary food may be safely accomplished.

After the stricture has been dilated to the maximum size desired, it is necessary to maintain the enlarged channel by passing the bulb last used every few weeks or months until the surrounding connective tissue becomes mature. The use of the dilating bulbs may then be discontinued entirely.

Experience has abundantly demonstrated that subsequent to a year or two of proper management there is very little and finally no tendency for the lumen of the esophagus to become narrower. Adopting the same

method the writer has successfully dilated narrow strictures located in the upper portion of the stomach not considered amenable to the usual surgical procedures. The bulbs on the flexible wire may be safely pushed through extremely tortuous channels if one is content with small gains at each dilatation.

In selected cases, particularly if one has had considerable experience in esophageal work, a piano wire guide may be introduced without the aid of the silk thread. It is always much safer, however, to use the thread as a guide. A baby eighteen months old, with an exceedingly tight stricture extending the entire length of the esophagus, caused by swallowing lye, was able to swallow the thread. In some instances, however, the patient comes under observation at a time when the stricture is so tight and starvation so far advanced that even the delay of a few days may be dangerous. An expert may then be able safely to pass fine filiform bougies or hairlike wires armed with minute bulbs and accomplish dilatation over these guides, and thus spare the patient the inconvenience and danger of a gastrostomy.

After years of experience in esophageal work the writer has perfected and adopted this method of dilating organic esophageal strictures. When pressure is required one knows that the point of the dilator is directly in the channel of the stricture and that it cannot go astray. The sense of security experienced in applying the method is exceedingly gratifying. The danger of making a false passage by forcing an unguided bougie down the throat of a confiding patient is practically eliminated. The most tortuous strictures are dilated with the minimum of traumatism. Carcinomatous strictures are treated with increased safety.

CARCINOMA OF THE ESOPHAGUS

Carcinoma is the most common serious disease of the esophagus. Compared with carcinoma of other organs, the esophagus stands fifth in frequency. The disease occurs chiefly between the ages of forty and sixty, and more frequently in men than in women. About 50 per cent are located at the lower end of the esophagus; 40 per cent at or near the bifurcation of the trachea, and 10 per cent in the cervical portion of the esophagus.

The growth usually surrounds the esophagus and may extend along the course of the tube from 1 to 5 inches. Its tendency is to produce stenosis and break down in ulceration. Gangrenous sloughing of the exposed surface of the tumor is common. Metastatic growths develop in the bronchial glands, liver, cervical glands, pleura, lung, and other organs. The pericardium and thoracic blood-vessels may be invaded.

Extensive metastases are relatively late and are frequently not dem-

onstrable during life. There is little tendency to the development of dilatation of the esophagus above the seat of a carcinomatous stricture. The course of the disease is progressive. The duration varies with the tendency to early obstruction and such accidents as perforation. The early stages may be slow in development. After the first symptoms of difficulty in swallowing become manifest, the average duration of life is six or eight months. Death may occur within a few weeks, and is rarely delayed more than from twelve to fourteen months.

General Treatment.—The location of the disease, the degree of stenosis, the probable duration of the disease, the general condition of the patient, must be carefully considered. These factors, combined with a knowledge of what may be accomplished by palliative treatment and by radical surgical measures, should leave no doubt as to the course to be pursued in a given case. The surgical treatment of carcinoma of the esophagus is confined to resection, esophagostomy, and gastrostomy. Only a relatively small number of growths are located in the cervical region, where they are accessible to radical operation. There is reason for hoping that within a few years operations on the thoracic portion of the esophagus may be performed with a much greater degree of safety than at present. The tissues of the thorax in the neighborhood of the esophagus seem to have little resistance to the character of infection that is likely to develop when the esophagus is opened. At present resection of the esophagus and esophagostomy are limited to very rare and selected cases.

Gastrostomy has a legitimate, although rather restricted, application in the treatment of carcinoma of the esophagus. As a rule, the operation should not be performed as long as a sufficient quantity of nourishment can be given by mouth to prevent the patient from losing in weight more rapidly than would naturally result from the destructive action of the carcinoma. With rare exceptions, the careful use of the dilating bulbs, with or without X-ray or radium, as described, will render the operation unnecessary. Unusual pain, hemorrhage, or inflammatory reaction following the use of the bulbs may justify gastrostomy. The operation is of the greatest value in those cases in which a high-grade obstruction of the esophagus occurs relatively early in the course of the disease, and unusual difficulty is experienced in maintaining an adequate opening through the stricture by the careful use of dilating instruments. If perforation into a bronchus occurs, gastrostomy may be justified. The duration of life, however, after such an accident is usually very short as pulmonary infection generally develops.

Palliative Treatment.—The great tendency of a carcinomatous growth of the esophagus is to obstruct the lumen of the tube and cause death from starvation. Since it is practically impossible to eradicate the disease, the chief indication in treatment is to provide nourishment and add to the comfort of the patient by treating the symptoms as they arise. In

selected cases X-ray and particularly radium may be used to retard the development of the growth.

A sufficient quantity of nourishment can be supplied only through the natural channel or a gastrostomy opening. Palliative treatment seeks to prevent the growth from obstructing the lumen of the tube. Inflammatory swelling and spasm are often important factors in contributing to the obstruction. Autopsies on cases in which the obstruction during life seemed almost or quite complete usually show a surprisingly large opening through the tumor mass.

If the nature of the disease is discovered before the stenosis has become pronounced, it is usually possible to prevent the lumen of the tube from becoming obstructed sufficiently to cause death from starvation. The chief aids in overcoming the obstruction are dilating bougies, appropriate diet and the use of radium in selected cases.

The method advised for dilating strictures due to cicatricial stenosis, already described, is largely applicable to the dilatation of carcinomatous strictures. Owing to the friability of the carcinomatous tissue and consequent danger of tearing and perforating the wall of the esophagus, the silk thread and piano wire guide are to be particularly recommended. A sufficient number of conical bulbs of gradually increasing size should be threaded on the flexible wire guide both in front and behind the dilating bulb to insure the minimum degree of traumatism.

As a rule, the carcinomatous tissue yields readily to the dilating force. The danger from hemorrhage and reactionary inflammation is greatly reduced if one is content with a small gain each treatment. The most satisfactory results are usually obtained by dilating only once each week. By gradually enlarging the opening one may finally succeed in passing a bulb 40 mm. in circumference. Cases apparently on the verge of starvation may thus be enabled to take a sufficient quantity of nourishment until death occurs from causes other than starvation.

Other mechanical means have been employed to prevent the tumor mass from obstructing the lumen of the esophagus. Leyden and Renvers used graduated hard rubber cannulas. It is doubtful whether the use of such agencies is justified.

Diet.—In all cases the diet should be non-irritating and contain a sufficient quantity of nourishment. If the disease is discovered before obstruction is pronounced, a gain in weight may be accomplished by giving a quart of milk and a pint of cream each day, together with soft toast, rice, oatmeal, vegetable purées, soft eggs, and scraped beef. All coarse and irritating foods should be avoided. The diet should be as varied as possible, as long as the lumen of the esophagus is adequate. As the obstruction increases it usually becomes necesssary to confine the diet entirely to liquids. Then milk, cream, koumiss, beef tea, and raw

eggs should form the basis of nourishment. The deficiency in carbohydrates may be supplied in part by adding grape sugar.

A man weighing 160 pounds will be adequately nourished if able to take each day 24 ounces of milk, 24 ounces of cream, 4 eggs, and 3 ounces of grape sugar. The eggs may be beaten up with the milk and the grape sugar dissolved in a portion or all of the mixture. The quantity of nourishment may be so divided that the same amount is given every two hours.

As the obstruction increases, regurgitation may be reduced to the minimum by administering the nourishment in tablespoonful doses repeated frequently until the full quantity, or as much as possible, has been taken. Aversion to the continued use of milk and cream diet may be greatly overcome by giving it at different temperatures and changing its flavor by adding small amounts of coffee, tea, or chocolate. A taste of the various fruit juices or a bit of cracked ice after each feeding increases the tolerance of a liquid diet.

During the course of the disease sudden narrowing of the lumen of the esophagus may arise from acute inflammatory swelling. Deglutition becomes unusually difficult and painful. The passage of the dilating bulbs causes unusual pain. Both pain and obstruction may be greatly relieved by giving the esophagus absolute rest and substituting rectal feeding for a period of two or three days. The diet should then be restricted to liquids entirely for a few days at least.

If, notwithstanding the use of dilating bulbs, appropriate diet, and the other measures advised, regurgitation of food takes place to such an extent that the patient is inadequately nourished, as shown by a rapid loss in weight, great thirst, and a reduction in the daily quantity of urine to less than 1 pint each day, death will soon take place unless relief is afforded by gastrostomy. If gastrostomy is contra-indicated, the intense thirst may be greatly relieved by the use of saline enemas.

SPASM OF THE ESOPHAGUS

Tonic or intermittent contraction of the muscular fibers of the esophagus resulting in uncomfortable deglutition may take place at any point in the esophagus. Spasm sufficient to cause obstruction, however, rarely occurs excepting at the upper and lower ends of the esophagus. The following groups of cases may be distinguished: (1) Esophageal spasm occurring as a symptom in well-recognized diseases, such as tetanus, hydrophobia, hysteria, chorea, epilepsy. (2) Esophageal spasm resulting reflexly from disease located in the esophagus or elsewhere in the body, such as tubercular ulcers of the larynx, disease of the stomach, peritoneum, and uterus. (3) Esophageal spasm occurring without apparent cause.

In such cases ill-defined nervous states are likely to be present. The familiar globus hystericus is said to be due to esophageal spasm. Spasm of the esophagus rarely causes serious symptoms except when located at the pharyngeal or cardiac orifices. Spasm of the pharyngeal orifice rarely causes serious obstruction. As a rule, it may be overcome by the passage of large-sized bougies. In a case under observation recently no improvement was noted until the orifice was forcibly stretched by the rubber bag dilator described in the treatment of cardiospasm. Spasm of the esophageal muscle occurring at points between the pharyngeal and cardiac orifices seldom requires treatment. If troublesome, the systematic passage of bougies is usually followed by satisfactory results. Bromids may be given advantageously. The underlying condition should be sought, and, if possible, removed. Spasm at the cardiac orifice will be discussed under the following heading:

Idiopathic Dilatation of the Esophagus

(*Cardiospasm*)

Dilatation of the esophagus arising independently of obstruction by an anatomical narrowing of its lumen was first described by Purton in 1821. In 1874 Ziemssen and Zenker collected from the literature 17 cases. The early cases reported were discovered postmortem. Recently the disease has been recognized ante mortem and has been treated successfully. Although 30 years ago so-called idiopathic dilatation of the esophagus was looked upon as rare, chiefly of pathologic interest, and scarcely to be diagnosed ante mortem, we now know that the condition is undoubtedly not rare and is sufficiently grave to demand a more widespread knowledge of its manifestations and treatment. The writer has recognized and treated over 300 cases since 1903.

Etiology.—The following factors are recognized as contributing to the development of so-called idiopathic dilatation of the esophagus:

1. Primary cardiospasm (Mikulicz and Meltzer).
2. Primary atony of the musculature of the esophagus (Rosenheim).
3. Simultaneous development of cardiospasm and paresis of the musculature of the esophagus due to anatomical or functional disease of the pneumogastric nerve (Kraus).
4. Congenital malformations (Fleiner).
5. Primary esophagitis (Martin).

The writer believes that the term cardiospasm as applied to this condition is likely to be misleading. There is but little evidence that heightened or spasmodic contraction of the muscle at the cardiac orifice of the esophagus is either the essential cause or a necessary factor in the de-

velopment of the disorder. The normal resting esophagus is empty, except for a narrow column of air retained by a firm closure of both orifices maintained by a contraction of the circular muscle fibers of the esophagus at these points. It is estimated that the closure of the cardiac orifice thus maintained is firm enough to support a column of water two-thirds the height of the esophagus. Normally the contraction of the circular muscle fibers at both orifices is automatically relaxed during the act of swallowing, allowing food and drink to pass unhindered into the stomach.

If the neuromuscular mechanism of the esophagus is disturbed in such manner that upon swallowing the normal automatic relaxation of the cardiac orifice fails to take place, food and drink may become arrested and retained in variable quantities in the lower portion of the esophagus, without heightened contraction or spasm of the muscles at the cardiac orifice. It is conceivable that the stagnation of food thus retained may give rise to irritation and thereby reflex spasm of the circular muscle fibers of the cardiac orifice, thus increasing the resistance to the passage of food. While it is apparent that spasm of the muscle at the cardiac orifice is not necessarily a primary or secondary factor in the development of the condition, as yet one is not justified in assuming that spasm of these muscles as a causative factor may be denied and entirely disregarded in the treatment of the condition. The writer believes that in advanced cases angulation of the esophagus as it passes through the diaphragm contributes to the development of the dilatation and the persistence of the small degree of retention that is often observed even after the cardiac orifice has been adequately stretched.

Anatomically two forms of idiopathic dilatation of the esophagus may be distinguished: (1) fusiform dilatation with marked hypertrophy of the muscle wall of the esophagus, (2) dilatation with slight or no hypertrophy of the esophageal muscle.

The first is the common form. The second is favored by atony of the muscle wall and a rapid accumulation of food, stretching the esophagus before muscular hypertrophy has had time to develop. The degree of dilatation varies, being greatest when the esophageal wall is atonic. The capacity of the normal esophagus is about 100 c.c. Kinnicut demonstrated a specimen in which the capacity of the dilated esophagus was 1,800 c.c. In the majority of cases the capacity of the dilated esophagus does not exceed 500 or 600 c.c. In a fatal case observed by the writer the dilated esophagus held 500 c.c. The hypertrophied muscle was 9 mm. thick. The normal thickness of the muscle of the esophagus varies from 1 to 2½ mm.

Pathological specimens show no evidence of hypertrophy of the musculature at the seat of the obstruction. The hypertrophy is compensatory and therefore develops in the sac above the obstruction. Very little force effectively applied is required to overcome the slight resistance of-

fered to the entrance of food into the stomach. The powerful contractions of the hypertrophied muscle of the dilated esophagus, however, fail to empty the esophagus completely, because there is less resistance above, consequently a portion or all of the contents of the esophagus may be forced upward. The more fluid the contents, the more readily they are propelled upward. As more food or fluid is introduced into the esophagus, the added pressure from above aided by such imperfect relaxation of the constricting fibers at the cardiac orifice as may take place during the act of swallowing causes a portion of the esophageal contents to escape into the stomach. A variable quantity of food and fluid mingled with tenacious mucus is more or less constantly retained in the esophagus. Eventually the retention results in dilatation of the esophageal tube.

The dilatation is usually fusiform, terminating at a point about 3 cm. above the cardiac orifice of the stomach. The seat of the greatest dilatation is in the lower third of the esophagus. The mucous membrane of the sacculation rarely shows much increased redness or other evidence of irritation due to the stagnation of food.

Diagnostic Aids.—Nearly all of the usual signs of esophageal obstruction from organic stricture are present. The following peculiarities, however, may be observed in stenosis due to cardiospasm: (1) Great fluctuation in the course of the disease. Years may elapse before emaciation appears. (2) Difficulty in swallowing liquids may be greater and appear earlier than the difficulty in swallowing solids. (3) The degree of dilatation of the esophagus may be much greater than that which occurs from organic stricture. (4) The obstruction to the passage of liquids is more complete than that caused by organic stricture. It may be possible to aspirate from 100 to 600 c.c. from the esophagus, hours after the liquid is swallowed. Except when spasm or acute inflammatory swelling complicates an organic stricture, a sufficient opening is practically always present to allow liquids to trickle through. (5) Upon passing a stomach tube or large-sized bougie it may be temporarily arrested at the cardia and then passed on into the stomach. In some cases there is no obstruction to the passage of the bougie, although food and liquids are retained in the esophagus.

Roentgen ray examination shows retention of barium solution in the esophagus. The lower portion of the elongated shadow gradually tapers to a point below the diaphragm. Irregularities commonly seen in the barium shadows when the obstruction is caused by carcinoma or cicatricial narrowing at the cardiac orifice of the stomach are absent.

The onset of symptoms may be sudden or gradual. In most cases the first symptom noted is discomfort or real pain located beneath the lower part of the sternum occurring during the ingestion of food or drink. A choking sensation causes the patient to eat slowly. In mild cases there may be no other symptoms, and the condition may disappear without

further development. In the more serious cases regurgitation of food and mucus takes place, and starvation is threatened. Finally, death may result if the obstruction is not relieved. The earlier the condition is recognized the more favorable the prognosis. After dilatation of the esophagus has taken place it is improbable that it ever regains its normal size. Symptoms of the disorder have continued for twenty years. Other cases have advanced to a fatal termination in two or three years.

Treatment.—In mild cases it may be sufficient to give soft warm non-irritating diet, combined with bodily and mental rest. Foods should be taken slowly; chemical, mechanical and thermal irritants should be avoided. Cold drinks are likely to increase the difficulty. Bromids may aid in controlling the condition. Temporary improvement in swallowing is often noted after the passage of the stomach tube or the use of an ordinary esophageal bougie. In some cases, particularly in those in which the lower end of the esophagus is inflamed or eroded, the use of the stomach tube or bougie may cause great pain and be followed by an increase in the difficulty in swallowing. To overstretch the muscle fibers at the seat of the obstruction is the best treatment as yet devised. While large bougies give temporary relief in some cases, no actual stretching of the cardiac orifice is accomplished.

Mikulicz conceived the idea of making an opening into the stomach and then forcibly stretching the cardia from below by means of an instrument acting in the manner of a uterine dilator. The success obtained by Mikulicz in the 4 cases thus treated by him has led others to adopt the same method. While the procedure is not particularly difficult or dangerous, it must be classed among the major operations and is no longer justified.

In 1903 [1] the writer devised a rubber bag dilator by means of which the same degree of dilatation may be obtained without subjecting the patient to the risk of a serious surgical operation. An anesthetic is not required, and the discomfort is little more than that which attends the passage of a bougie. The instrument as now constructed consists of a thin rubber bag 5 inches long and 1½ inches wide when collapsed. At one of the upper corners of the bag firm rubber tubing about 20 inches long is attached through which the bag may be distended with air under measured pressure. Another piece of rubber tubing 6 inches long is secured in the center of the bag. A special whalebone introducer is passed through the channel thus created. A metal conical bulb provided with a lateral canal for the passage of a silk thread guide is screwed to the slightly projecting lower end of the whalebone introducer. A thin, firm silk or linen bag 7 inches long and of the required width surrounds the rubber bag in such a manner that when the rubber bag is distended

[1] Since that time Plummer and others have devised excellent dilating bags similar in principle.

with air a firm cylinder is produced about 5½ inches long and of the circumference of the cloth bag selected for use in dilating the esophagus in a given case. When collapsed, ready for introduction, the diameter of the instrument is less than that of an ordinary stomach tube (see Fig. 3).

To facilitate the passage of the instrument an ordinary rubber condom is drawn over the cloth bag and secured by a thread ligature. The long rubber tubing is connected with an ordinary clinical blood-pressure apparatus so that the pressure used in distending the bag may be accurately measured. Before introducing the instrument the bag should be distended by the pressure that is to be used and the circumference of

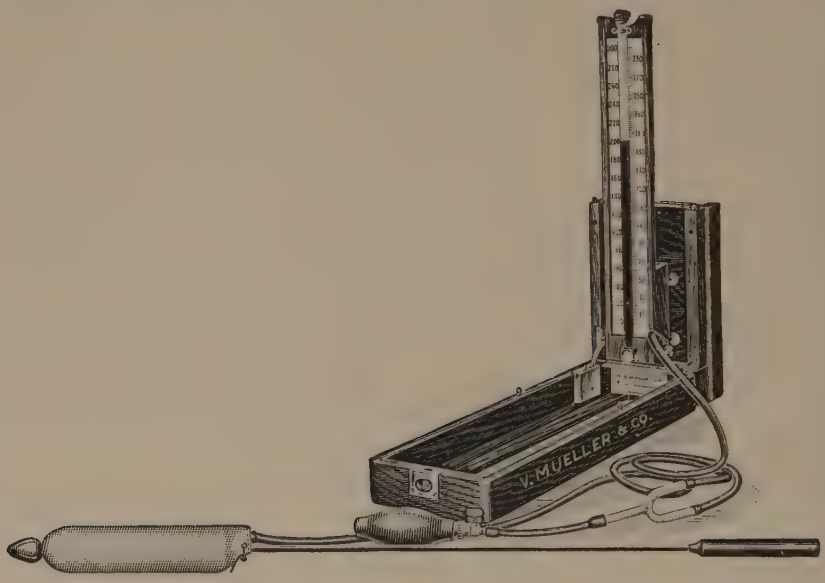

Fig. 3.—Collapsible Rubber-bag Cardiospasm Dilator. (Sippy.)

the bag thus distended should be measured. The size and distensibility of the lower end of the esophagus varies. In dilating it, extreme caution must be used, as the esophagus has been ruptured by the simple act of vomiting and the passage of an ordinary stomach tube. As a rule, at the first dilatation, it is safe to use a cloth bag that limits the circumference of the dilating instrument to 4 inches, when distended by an air pressure of 200 mm. mercury as measured by the clinical blood-pressure apparatus. Bags permitting greater dilatation are usually required so that a series of cloth bags ranging from ¼ to ½ inches larger in circumference should be ready for use at subsequent dilatations if required.

In rare instances adequate dilatation has not been accomplished until a bag producing a cylinder 7½ inches in circumference has been used.

Ordinarily the instrument can be properly introduced without the use

of the silk thread as a guide. There are cases, however, in which the sacculation is so great that the bulb of the introducer becomes arrested at the bottom of the sac and fails to find its way through the cardiac orifice. It is advisable, therefore, in all cases to make use of the silk thread guide swallowed and anchored as described for use in dilating organic strictures of the esophagus.

The instrument is introduced by passing the free end of the anchored thread through the lateral canal of the conical bulb screwed to the lower end of the whalebone introducer. The thread is then pulled taut and the collapsed bag lubricated with olive oil is guided into the cardiac orifice. In a patient of average height the cardiac orifice is approximately 16 inches from the incisor teeth. It is well to introduce the bag 1 or 2 inches deeper and then withdraw it so that the teeth are at a point previously marked on the whalebone staff by a narrow adhesive strip, 16 inches above the center of the dilating bag. If desired, the location of the bag may also be determined by noting the position of the conical bulb by fluoroscopy.

Holding the whalebone firmly so that the incisor teeth are at the 16-inch mark, air is pumped into the dilating bag until the mercury rises to 100 mm. Unless serious pain is produced, the pressure should be gradually increased until the mercury rises to 150 or 200 mm. If the center of the bag is too far below or above the correct point in the cardiac orifice, as the bag is distended the whalebone staff is drawn downward or pushed upward. When in the correct position there is very little tugging on the staff in either direction. Rarely greater pressure may be employed. The amount of pressure required to overstretch the thin muscle at the cardiac orifice is small, provided the cloth bag is of proper size. If the cloth bag is too large for a given case, a pressure greater than 200 may rupture the esophagus. Improper use of any dilating device may result in death or in the production of an organic stricture.

It must be remembered that, the greater the circumference of the cloth bag when distended, the greater the degree of lateral or stretching force exerted by the same degree of pressure as registered by the mercurial or Tycos manometer. Proper stretching is accompanied by definite discomfort, but rarely by severe pain. The pressure should be maintained at the highest point for a few seconds, then the tubing should be disconnected and the air allowed to escape. Without withdrawing the bag it is usually advisable thus to distend the bag in correct position two or three times after which the collapsed instrument is withdrawn. As a rule, if the stretching has been adequate, slight traces of blood are seen on the bag. The effect of the stretching may be tested at once by asking the patient to drink water. If very definite improvement in swallowing is noted, the cardiac orifice has been actually stretched, although perhaps not sufficiently. The degree of improvement in swallowing combined with

fluoroscopy the following day will determine whether the bag 4 inches in circumference was large enough. As a rule, larger bags are required, but it may be disastrous to stretch the esophagus beyond the extent advised until it has been demonstrated that greater stretching is necessary or permissible.

For the sake of convenience the rubber bag dilator may be surrounded first by a silk or linen bag which limits the circumference of the distended bag to 7½ inches. The ends of the retaining bag should be adjusted in such a manner as to prevent rupture of the rubber bag. The series of cloth bags advised may be of simpler construction in that they do not require careful adjustment of the ends to the rubber bag. A cloth bag of appropriate size is drawn over the collapsed larger bag, thus limiting the circumference of the dilating instrument to the size desired. When collapsed, the outside bag is easily withdrawn and replaced by one larger in circumference if required.

Influenced by the pain, bleeding, improvement in swallowing resulting from each stretching and other factors peculiar to the individual case, cloth bags of larger circumference may be substituted for the cloth bag previously used until the stretching of the cardiac orifice has been adequate. This is shown by complete comfort in swallowing and the absence of barium retention on fluoroscopy observed the following day. When the sacculation is extreme, a quantity of barium may cling to the folds of the esophagus even though the cardiac orifice has been adequately stretched. Such retention does not give rise to subjective symptoms.

No very special after treatment is required. Cold drinks should be avoided and a non-irritating diet employed. One adequate stretching is likely to suffice for years. A record of the circumference of the dilating bag last used should be kept to facilitate subsequent dilatations when required. The principle of the urethral dilator has been utilized and long instruments constructed by means of which the cardiac orifice has been stretched. The esophagus varies in size and distensibility. It is obviously dangerous to stretch the esophagus to a given circumference without measuring the force that is being used.

DIVERTICULA OF THE ESOPHAGUS

An esophageal diverticulum is a pouch-shaped sacculation involving a limited portion only of the circumference of the esophagus. The condition is sharply differentiated from dilatation of the esophagus, in which the entire circumference of the tube is involved. The wall of the pouch usually consists of mucous membrane and connective tissue, the muscular coat of the esophagus having been either destroyed or pushed aside.

The mucous membrane of the sac is usually only slightly altered. Deep erosion or ulceration is rare. Carcinoma may develop as a result of local irritation. According to the manner in which the pouchlike sacculation develops, three types are recognized: pressure or pulsion diverticula, traction diverticula, and traction-pressure or traction-pulsion diverticula.

Pressure diverticula, though less common than *traction diverticula,* are of much greater clinical interest. They may be located (1) in the pharynx; (2) at the junction of the pharynx and esophagus; (3) near the bifurcation of the trachea, usually just above the left bronchus; (4) below the level of the left bronchus.

Congenital defects may contribute to the development of a pressure diverticulum. A large bolus of food may lodge in the pharynx or esophagus and cause a slight stretching or bulging of a circumscribed area. Subsequently food may accumulate at this point, exert pressure, and finally cause the formation of a pouch. The most common and important pressure diverticula develop immediately below the junction of the pharynx and the esophagus. At this point there is a natural weakness of the muscular structure. The capacity of the pouch of a pharyngoesophageal diverticulum varies from a few cubic centimeters to 250 and more. They usually originate in the median line posteriorly. As the pouch develops it usually pushes the esophagus aside and occupies a left lateral position.

Owing to pressure exerted by the left bronchus against the esophagus, food may lodge on the wall of the esophagus just above the bronchus and cause sacculation. Pressure diverticula below the level of the left bronchus are exceedingly rare.

Traction diverticula are common but rarely seen except at autopsy. The local bulging is nearly always due to contraction of scar tissue attached to the outer surface of the esophagus. The cicatrix usually arises from inflammation of bronchial lymph glands in the vicinity of the bifurcation of the trachea. Hence traction diverticula are frequent in tuberculous subjects. They are usually funnel-shaped and remain small if the mouth of the pouch is lower than its cavity, thus preventing the accumulation of food.

As a rule, traction diverticula produce no symptoms, except when associated with suppurative processes. Rupture may then take place into the surrounding organs, as trachea, bronchi, pleura, and blood-vessels, with disastrous results.

A *traction-pressure diverticulum* may develop when the orifice and sac of a traction diverticulum favor the entrance and accumulation of food. A traction-pressure diverticulum may become large and correspondingly serious. This type is exceedingly rare.

Course.—Symptoms of importance rarely develop before the age of fifty, except when the condition originates from a congenital stenosis of

the esophagus. For years the patient may be conscious that food lodges at a certain point in the esophagus. Symptoms similar to those of a gradually increasing stenosis may subsequently appear and slowly develop until, finally, death from starvation or intercurrent disease takes place, unless the condition is relieved.

Diagnosis.—With the aid of the X-ray the diagnosis is extremely simple. The pouch invariably fills with barium, revealing the location and extent of the sacculation. Herniation of a portion of the stomach through the diaphragm may give X-ray evidence simulating a diverticulum of the lower end of the esophagus. Error in diagnosis from that source may be excluded by understanding that a diverticulum at that point of any considerable size virtually never occurs, and that if carefully observed the barium may be seen going through the diaphragm before it enters the sac above the diaphragm. Also at times peristaltic waves may be seen in the pouch caused by the herniated portion of the stomach.

Treatment.—If the condition develops late in life, and little or no hindrance to the passage of food is present, the patient should be directed to eat slowly and avoid coarse foods. Appearing thus late in life, even though it is impossible to pass a tube into the stomach, serious symptoms may never develop. If serious difficulty begins earlier in life, the disorder is likely to result in death unless more active measures are instituted. It should be more widely known, however, that the pouch of a diverticulum of the esophagus is likely to develop slowly, and that an untreated diverticulum seldom causes death except through starvation. Starvation rarely, if ever, occurs except when the pouch becomes so large the food accumulating in it causes the sac to crowd against the esophagus, narrowing its lumen, thus preventing the entrance of food into the stomach. As a rule, many years elapse before a diverticulum of the esophagus becomes large enough to cause serious difficulty in swallowing. Fortunately the most common diverticula, those developing at the upper end of the esophagus, are amenable to surgical treatment. In properly selected cases operative treatment is indicated. Virtually all mortality from the operation may be avoided by not cutting off or opening the sac. Owing to the poor blood supply of the walls of the sac, leakage from the esophagus is liable to occur. The tissue in that territory seems to have little resistance to such infection. In the service of the writer since 1906 the sac has been disposed of without opening it. Diverticula having their origin below the sternal notch are usually inoperable. Fortunately they seldom become large enough to be of clinical importance. In many cases, the position assumed by the patient while eating or drinking influences greatly the permeability of the obstruction. Many different lateral and other positions should be faithfully tried until the one most favorable to swallowing is found. In some cases swallowing is best accomplished when the stomach is higher than the mouth, so that food and drink are

forced upward entirely by peristaltic action. If starvation threatens, the silk thread introduced in the manner as advised for dilating esophageal strictures is likely to be of inestimable value. The thread when swallowed may become arrested temporarily in the pouch. Within a reasonable time, however, it floats into proper position and is then carried on into the stomach and becomes anchored in the intestine. The thread thus serves as an accurate guide into the esophagus beyond the pouch and may be used in many ways to overcome the difficulties in an individual case. For example, by using the thread as a guide, flexible tubes may be introduced into the esophagus beyond the pouch, enabling one to convey abundant nourishment to the stomach. It should seldom become necessary to perform gastrostomy.

FOREIGN BODIES

Foreign bodies of various kinds become impacted in the esophagus, causing serious symptoms, and, unless properly managed, death may result. The accident occurs most frequently in children, although adults are by no means exempt. The natural tendency for a baby to put everything possible into its mouth is responsible for many cases. Coins, buttons, buckles, peach stones, and open safety pins are among the common objects swallowed. Adults accidentally swallow false teeth, bones, and peach stones. Rarely other foreign bodies become lodged in the esophagus.

It often happens that in swallowing a small foreign body slight traumatism of the esophagus occurs, and, although the object has passed on into the stomach, the patient declares it is lodged at the seat of the traumatism. It is important to know the shape and character of the foreign body. Unless it is perfectly obvious that the object could not become impacted it should not be assumed without proper investigation that it has not lodged somewhere in the esophagus. I wish particularly to warn against the common practice of assuring frightened mothers that pennies and similar objects will always pass without doing harm. It is true that in most cases a penny does not give rise to trouble. To my personal knowledge, however, many deaths have resulted from this cause. The penny usually lodges in the upper end of the esophagus at a point just below the cricoid cartilage. Relatively few symptoms may be present at first. For two or three days the baby may be able to swallow its liquid nourishment. Pressure necrosis is followed by inflammatory swelling and the wall of the esophagus sloughs and the penny may escape into the periesophageal tissue. Death from infection follows, unless prompt surgical relief is instituted. At best, the mortality is high following infection through a sloughing esophagus. The earlier the attempt is made to

remove the foreign body, the greater the likelihood of success. Inflammatory swelling always develops sooner or later from infection due to abrasions caused by the foreign body or to pressure necrosis. The resulting edema increases the difficulty of removing the object. When there is doubt as to whether a foreign body, such as a penny, brass button, or safety pin, has passed, an X-ray plate or fluoroscopic examination should be made. If the object is located, its projecting angles should be noted. It may be possible to seize the object with specially constructed esophageal forceps and withdraw it by the aid of the fluoroscope. In other cases the

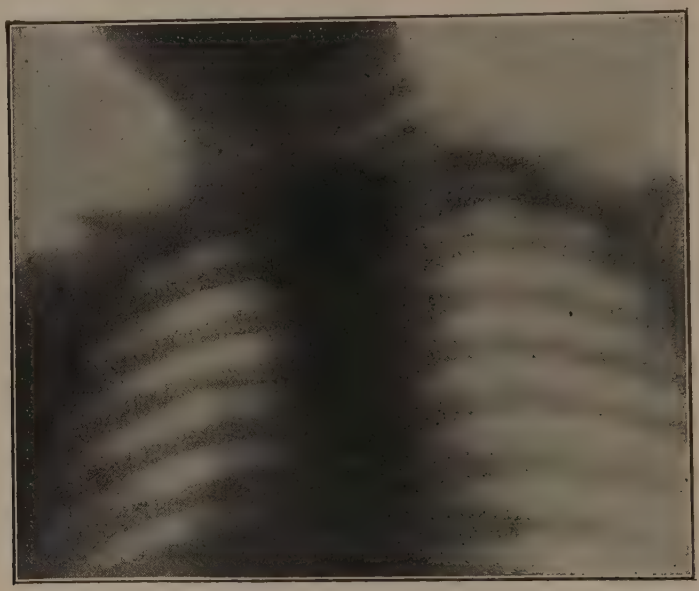

Fig. 4.—Penny Impacted in Esophagus of Child Two and a Half Years Old. Usual Position. Removal after seven days. (Sippy.)

esophagoscope may be passed and the foreign body grasped by long esophageal forceps working through the esophagoscope.

It often happens that, unless care is exercised, a foreign body located in the upper end of the esophagus is dislodged by the esophagoscope. In such cases evidence of pressure necrosis may show where the body is located. The whole length of the esophagus should then be explored. The dislodged foreign body is often arrested at the lower end of the esophagus. It will usually be free and easily grasped and drawn out as the esophagoscope is withdrawn.

The seriousness of delay in the removal of foreign bodies from the esophagus cannot be too strongly emphasized. Early attempt at removal by a reasonably skillful man should be successful. The longer the delay, the greater the difficulties and dangers experienced.

ACUTE ESOPHAGITIS

Acute inflammation of the esophagus of such intensity as to cause symptoms is relatively rare. The most common cause is the ingestion of chemical and corrosive substances. Under ordinary conditions acute inflammation of the stomach, pharynx, larynx, or trachea is seldom transmitted to the esophagus. Acute general diseases and infections are now and then associated with a mild esophagitis. Croupous and necrotic inflammation of the esophagus is recognized as a very rare complication of typhoid fever, cholera, small-pox, measles, scarlet fever, sepsis, and uremia. In such cases there may be a direct extension of the inflammation from the pharynx or larynx. It is noteworthy that diphtheria rarely extends into the esophagus. Phlegmonous inflammation of the esophagus is extremely rare. Foreign bodies arrested in the esophagus may cause pressure necrosis and periesophageal abscess formation. Thrush may invade the mouth, pharynx and esophagus at the same time. In adults the growth of microörganisms is seldom sufficient to cause dysphagia. As a rule, the infection is found associated with such processes as typhoid fever, sepsis, and advanced tuberculosis. [2]

A burning sensation in the esophagus, pain upon swallowing, regurgitation of food, tenderness on pressure, are among the chief symptoms of simple esophagitis. Special etiologic factors and diseases of which esophagitis is but a complication influence the symptomatology.

Treatment.—In mild cases of acute esophagitis non-irritating foods, such as milk, cream, soft eggs, and gruels, may be taken. In severe cases all food and drink should be withheld for a few days, fluids being supplied in the form of salt solution per rectum. After a few days, milk, cream, olive oil, and other bland foods may be given. As a rule, local applications are unnecessary. If swallowing is not particularly painful, 1 or 2 ounces of a 5 per cent suspension of bismuth in water may be administered two or three times daily. Esophagitis from the swallowing of caustic chemicals may require morphin injections. If it becomes necessary to give fluids by mouth before the intensity of the inflammation has subsided, some relief from pain on swallowing may be obtained by giving a teaspoonful of a 1 : 1,000 solution of adrenalin containing 1 per cent cocain just before each feeding. The more intense the inflammation the greater the danger of subsequent cicatricial stenosis of the esophagus. Particularly in those cases in which corrosive substances have been swallowed esophageal bulbs should be passed as early as a week or ten days afterward. The patient should take a few swallows of olive oil just previous to the passsage of the bulbs. In severe cases the narrowing may

[2] In marantic children I have seen the esophagus blocked by a plug consisting principally of thrush.—Editor.

already be so great that only small-sized bulbs may be used. In a few days larger sizes should be used, gradually dilating every three or four days, until the maximum-sized esophageal bulb has been passed. This should be accomplished before extensive cicatricial narrowing has had time to develop. If the tissue destruction has been great it is often necessary to pass dilating bulbs, once each week for a few weeks; subsequently the intervals may be lengthened according to the requirements of the individual case.

ULCER OF THE ESOPHAGUS

Esophageal ulcer is not common. Among the causes may be pressure necrosis, the peptic action of the gastric juice, simple esophagitis, including the chemical action of corrosive substances, and sacculation of the esophagus with stagnation of food. Ulcer of the esophagus from tuberculosis, syphilis, and actinomycosis is extremely rare. Follicular ulceration may result from catarrhal inflammation of the mucous glands of the esophagus. This occurs chiefly in the aged. Local ulceration from the irritation of decomposing foods occurs in stricture and diverticula of the esophagus. Decubital ulcers may develop in typhoid fever and chronic tuberculosis. A perichondritis of the cricoid cartilage is usually present. The cartilage in contact with the esophagus is often hardened by calcific deposits. This, together with prolonged pressure due to horizontal position and contributory infection, may be sufficient to give rise to local necrosis. Ulceration of the esophagus not of the decubital type also occurs during the course of typhoid fever. Thyroid tumors may press the trachea firmly against the esophagus and cause ulceration. Aneurysm may cause pressure necrosis. Foreign bodies lodged in the esophagus may cause ulceration.

Peptic Ulcer.—Peptic ulcer of the esophagus is extremely rare. Less than 50 cases have been reported. A gastric ulcer may extend upward into the esophagus. The pure type of esophageal peptic ulcer, however, is confined to the mucous membrane and deeper tissues of the esophagus and occupies without preference any part of its lower third. Normally the gastric juice is prevented from coming in contact with the esophagus by a rather firm closure of the cardia. Insufficiency of the cardia allows the gastric juice to escape upward into the esophagus and peptic ulcer may result, provided the tissue of the esophagus through malnutrition or necrosis has lost its resistance to the peptic action of the gastric juice. Benign stenosis at the pylorus from gastric ulcer with retention of secretion, inducing more or less vomiting or regurgitation of gastric contents, has been causative of esophageal ulcer. Multiple ulcers of the stomach, duodenum, and esophagus have been observed. The disease is often latent.

The chief clinical manifestations are pain, dysphagia, vomiting, regurgitation, and hemorrhage. The ulcer may be demonstrated by the esophagoscope. Healing may take place with or without stenosis.

Tuberculous Ulcer.—In sharp contrast to the pharynx, larynx, large and small intestine, tuberculous ulcer is rarely found in the esophagus or stomach. Syphilitic ulcer of the esophagus is extremely rare, and only a few cases of actinomycosis of the esophagus have been reported.

Treatment.—The treatment of esophageal ulcer does not differ essentially from the medical treatment of gastric ulcer. It is impracticable to apply local remedies by means of the esophagoscope. If nutrition is seriously impaired or hemorrhage alarming, gastrostomy should be performed and the patient fed through the fistula until the ulcer is healed.

CHAPTER XXX

DISEASES OF THE STOMACH

JACOB KAUFMANN

REVISED BY ARNOLD GALAMBOS

INTRODUCTION

Every plan of treatment must be based upon a correct diagnosis and upon a proper understanding of the nature of the disorder and of the causes which provoke it. In discussing the treatment of gastric disturbances it seems, therefore, advisable to give a short sketch of the present views on the pathology of the stomach. A few general remarks are all the more necessary as the teaching regarding diagnosis and pathology of the stomach has undergone changes several times since Kussmaul in 1867 introduced the stomach tube and used it to study gastric function and gastric disorders. This change of view has usually been due to the overestimation of new findings; and since another change of view is taking place at present it is timely to take stock and see whether the new findings are being given their proper value.

First, let us emphasize the necessity and importance of systematic and thorough examinations of stomach contents; they are essential both to gain accurate knowledge of the condition of the stomach and to assist us in directing proper treatment.

It is sometimes said that the amount of information gained by gastric analysis is small and that one is easily led to an erroneous diagnosis by overestimating its value in comparison to other findings. In this, however, there is no difference between gastric analysis and other methods of examination. With any method of examination findings are of value only when taken in connection with the history of the case and all other clinical symptoms and, furthermore, when the findings are rightly interpreted. In case certain findings lead to an erroneous diagnosis we must not deprecate the method of examination, when in reality a faulty interpretation is the trouble. There is an abundance of proof of faulty interpretation of gastric analyses; a perusal of textbooks and current literature will con-

vince any critical reader that grave errors are often committed. This fact, however, should not make us desist from examining gastric contents, for a gastric analysis (when properly performed and interpreted) yields valuable information. Unquestionably the further development of gastric analysis will clear up features in the derangement of gastric function which at present are only poorly understood.

Progress in correct interpretation has principally been made in one direction, that is, regarding the relationship of motor and secretory disturbances, although there, too, much confusion still exists. For many years the chemistry of gastric digestion was the main object of examination, and abnormal findings were too readily attributed to derangements of the secretory function. Although the first and most important contributions to our knowledge of secretory disorders came from Kussmaul's Clinic, Kussmaul himself and his pupils always pointed to the greater rôle which the motor function plays in the pathology of the stomach. It was a long time, however, before most investigators could be convinced that even those conditions which appear to be entirely due to faulty secretion are to a great extent the result of motor disorders. For example, the clinical picture of continuous hypersecretion, formerly described by many as a pure secretory disturbance, is now generally considered as invariably connected with impaired motility and to a certain degree caused by the latter.

In our opinion what now-a-days is called alimentary hypersecretion is also wrongly interpreted as being mainly a derangement of secretion. Granting that there is an increased glandular activity, nevertheless we believe that the presence of the large quantities of fluid found in such cases can only be explained by a concomitant motor disturbance (pylorospasm or more frequently gastric atony), which allows its accumulation in the stomach.

The proper understanding of some of these conditions has been greatly improved by investigations on the nature of gastric peristalsis and the activity of the pyloric part of the stomach, notably, Dr. Cannon's work, which taught us that the rhythmic movement of the pyloric antrum and with it the evacuation of the stomach are regulated by the action of hydrochloric acid.

It must be said, however, that a defect in the secretion of hydrochloric acid does not necessarily upset the mechanism at the outlet of the stomach, as is shown in case of achylia with unimpaired motility. While this and other points still have to be cleared up, we believe that prolonged and increased secretion by irritating the duodenum may cause pylorospasm and by thus interfering with the evacuation of the organ lead to the accumulation of the secretion. In this way the clinical picture known as continuous hypersecretion and gastrosuccorrhea is developed. The same picture of retention of large quantities of secretion is produced when

pylorospasm is the result of some other cause than primarily increased glandular activity, for example, when it is the result of the irritating effect of perigastritis or adhesions. It is obvious how much the proper understanding of the development of such a condition must influence our plan of treatment.

Whenever the secretory disturbance is the primary factor we should try to remedy it by eliminating its causes: faulty habits, chronic intoxications, etc. If we do not succeed, or when, from the beginning, the motor disorder is the more important part, we should attempt to break the vicious circle by improving the evacuation of the stomach. When we are unable to accomplish this by medical means we must resort to surgery.

Operative treatment, however, should never be undertaken without at the same time using every effort to reduce gastric secretion to its normal limits. We must keep in mind that the gastric function is a complex mechanism, that one of its components cannot be disturbed without soon affecting another, that a motor disorder may upset secretion and vice versa, and that both in turn may derange evacuation and absorption.

Further to illustrate the great therapeutical value of reading correctly gastric analysis we mention those cases of hyperacidity in which the high degree of acidity is the result of hypermotility. The fast evacuation of the stomach brings about a high percentage of acids in the comparatively small amount of remaining contents, while the total quantity of secretion may have been small. Cohnheim of Heidelberg suggested lately that in such cases the administration of hydrochloric acid proves helpful by activating the lacking pyloric movements and by thus delaying the evacuation of the stomach—apparently a paradoxical proceeding, yet well supported by physiological facts.

Aside from the correct interpretation of disorders of the gastric function we have to consider their pathological meaning. Here again we meet with repeatedly changing views.

When gastric contents were first studied the mistake was frequently made of designating as a disease every change of gastric function elucidated by these methods. Up to the present time textbooks describe achylia gastrica, hyperacidity, hypersecretion, etc., as diseases per se. These and other functional disorders may be of independent character, but as a rule they are only symptoms of a pathological condition, either of the stomach proper or of some other organ, or they are manifestations of systemic derangements. It is therefore not enough to examine merely the gastric contents, for gastric analysis alone rarely permits a complete diagnosis to be made, but we must consider every other symptom and the history of the case before we can give the gastric disorder its proper place in the clinical picture. Gastric disorders are found in many different conditions, and they are provoked by numerous causes. In spite of all that is at present said to the contrary the first place should be given to those dis-

turbances which are the result of pathological changes of the stomach proper. The stomach is constantly subjected to insults, which tend to disease by direct harmful action upon the viscus. Faulty habits in eating, indiscriminate selection of food, abuse of alcohol, tobacco, and the like create gastritis mucosa, gastritis acida, and other organic changes, and with them all the different disorders of the gastric function.

On the other hand, we must bear in mind that the stomach more frequently perhaps than any other organ is easily upset by derangements in other parts of the body. In trying to establish a successful treatment it is therefore not sufficient to determine the condition of the stomach proper, but it is necessary to make a complete investigation of the system in order to find out whether we are dealing with a primary local disease or whether the gastric disturbances are only secondary in nature and caused by diseases in other organs. We have to consider here functional and organic derangements of the nervous system, diseases of the blood, metabolic disturbances, acute and chronic infections and intoxications, diseases of the circulatory system, diseases of the kidneys, of the liver, of the abdominal organs and of the pelvic organs, and their activity under pathological as well as under physiological conditions. We know that distinct gastric disturbances arise with menstruation, pregnancy, and the menopause.

This short summary covers a very large field and shows that the physician who undertakes to treat gastric disorders must be thoroughly familiar with medicine in all its aspects.

The occurrence of secondary gastric diseases has long been understood, as is seen in writings of older clinicians. When I first listened to lectures on gastric diseases at Kussmaul's Clinic about thirty years ago my teacher always laid great stress upon elucidating the various primary factors in cases with secondary gastric disturbances.

Of late one special group of secondary gastric disorders has aroused a great deal of attention, that is, disorders caused by chronic appendicitis, diseases of the gall-bladder and the pancreas. Undoubtedly gastric disturbances are in certain cases brought on by reflex action from a diseased appendix or gall-bladder, and surgical interference may prove very helpful in the treatment of such conditions. We have no intention whatsoever of disputing such occurrences. In an article published some years ago J. Kaufmann was one of the first to discuss the frequent connection of gall-stones and gastric hyperacidity. But the frequency of such occurrences is greatly over-rated at present and too much importance is given to this special etiologic factor at the cost of others, which are well known as the causes of gastric disorders. If we want to believe all that is claimed at present, the large majority of all gastric disturbances have to be attributed to appendicitis, gall-bladder trouble, etc.

Even gastric ulcer is not considered a primary disease of the stomach

but only secondary to chronic appendicitis and the like. Accordingly, some surgeons counsel against performing gastro-enterostomy, once highly praised as the only rational treatment in gastric ulcer, and propose appendectomy or cholecystectomy as the most reliable cure of the tendency to pylorospasm, the dominating factor in many ulcer cases.

The difficulty is that, with the clinical picture clearly pointing to gastric ulcer, it is not at once evident from which other abdominal organ the reflex disturbance originates. If, for example, the diagnosis of chronic appendicitis is in such cases merely based on the most untrustworthy symptom, tenderness over McBurney's point, it often leads to the removal of an innocent organ in no way connected with the gastric symptoms. So it is also with many operations for assumed gall-bladder trouble. The frequent negative results of operations performed under such indications have brought forward the advice at the time of operation to examine all abdominal organs and correct every abnormality, lest the obvious may not be the real cause of the symptoms. This somewhat summary proceeding has certainly the advantage of sparing the patient the performance of a second, third, or fourth laparotomy, so often undertaken in the vain effort to find the real culprit. The search is made on the basis of wrong reasoning. Because in certain cases gastric disorders are provoked by appendicitis or gall-bladder troubles one is not justified in assuming that almost all gastric disturbances are due to such reflex action. While it is justly claimed that gastric analysis is of value only when properly interpreted and when taken in connection with the history and with all other clinical symptoms, we must ask the same for the valuation of anatomical findings gained at operations. The causal connection between anatomical findings and clinical manifestations must be demonstrated particularly by the further development of the case. The mere fact that at operation the appendix or other organs are found diseased does not prove that these changes are the causes of the gastric disturbances. That they are very often not the cause is amply demonstrated by the frequent failure of operative treatment to prevent the recurrence of the original gastric disturbance. Not a week passes but what we see patients who, on examination, present the scars of one, two, or more laparotomies performed for the very purpose of curing the patient of the gastric ailments for which he is still seeking relief. We are convinced that others meet with the same experience. Such patients continue to suffer for the very good reason that the operation did not remove the cause of their trouble, as was promised. This applies not only to the numerous instances where, on account of an erroneous diagnosis, the assumed anatomical changes were not present and no beneficial result could be expected, but also to those cases where anatomical alterations were actually found. In many cases of the latter group the real causes of the gastric symptoms are chronic colitis, hepatitis, cirrhosis of the liver, and other organic diseases of different abdominal

organs which are not touched at all by the operation. In another group of cases organic changes of the appendix, etc., have less harmful influence upon the gastric function than have constitutional derangements, faulty habits, or some other of the etiological factors mentioned above. These also remain unchanged by the operation. If, for example, the patient happens to be a neurotic and addicted to faulty habits he will have his gastric ailment after the operation in the same manner as he had it before.

The increasing number of unnecessary and unsuccessful operations makes us dwell upon this point, and we consider it timely to protest against a proceeding which has become quite common, that is, to take it for granted that chronic gastric disorders are almost invariably due to chronic appendicitis, gall-bladder trouble, and the like, a conception based on faulty and insufficient indications.

The presence of gastric ailments alone is not sufficient indication for operating on the appendix, the gall-bladder, etc. These operations should only be performed when the indication warrants the removal of the diseased organ (appendix, etc.) for its own sake. Furthermore, when in the latter group of cases gastric symptoms form a prominent part of the clinical picture, no positive promise should be given that the operation will also cure the disorders of the stomach. It may do so, but it just as often does not. The last word about the value of surgical treatment in the cases at issue will not be spoken by the surgeon, but by the medical man who has to attend the patient after the operation. Though we grant that, in a certain group of cases, chronic appendicitis and cholecystitis are the main causes of gastric disturbances, this does not entitle us to disregard everything else which we recognize as disorders of the gastric function. We get better and more lasting results by following physiological methods, by considering all etiological factors, and by devising a treatment which deals, as far as our knowledge goes, with constitutional shortcomings, systemic diseases, chronic intoxications, or whatever etiology the individual case may present.

In basing a plan of treatment on our knowledge of etiology with the intention of removing, if possible, the causes of gastric disturbances, we must not overlook the condition of the stomach proper. This applies not only to cases where the stomach is primarily diseased, due to faulty habits, but also to secondary gastric disorders. We cannot divide the system into sections and attend only to one part if ever so important as an etiological factor. We must take a broader view and consider the individual case in all its aspects. It is poor policy, for example, to claim that a neurasthenic should have treatment only for the derangement of his nervous system without taking any notice at all of his gastric symptoms. Very often gastric disturbances form a center of irritation for the nervous system, and their elimination greatly benefits the condition of the nervous system. Again, in incipient and advanced tuberculosis, proper attention and care

bestowed upon the frequently present gastric disorders will assist us in improving the nutrition of the patient, so essential in the treatment of tuberculosis. In heart cases with broken compensation the congestion of liver and stomach often provokes severe attacks of persistent vomiting, resembling conditions usually found in gastric ulcer. When treated accordingly by exclusive rectal feeding, not only the vomiting ceases, but the diminished congestion of the upper abdomen in turn greatly facilitates and improves the heart action, as we have observed in a number of cases. So it is also with other types of secondary gastric disturbance. We must always remember that gastric disorders influence the condition of other organs and the whole system just as much as vice versa. Æsop's fable of the belly and the members still holds true. We must make full use of all information gained by gastric analysis and other means in trying to correct disturbances of the gastric function by direct physical and medical treatment and by proper dieting. Every improvement thus accomplished will in turn benefit the underlying cause which provokes the gastric disorder.

In emphasizing the necessity of direct treatment of gastric disturbances, we are fully aware of the present tendency to belittle it, particularly on the part of surgeons, who, for example, allow their patients a liberal diet shortly after operations performed for the very purpose of curing gastric ailments. This utter disregard of the grave condition of the stomach, caused by the effects of narcosis and operation, is bound to do harm even to a previously normal stomach, as is shown by the sufferers who date the beginning of their stomach trouble to the time of an operation. On the other hand, proper regard for the rôle which secondary gastric disturbances often play in the development of a vicious circle always proves a great help in the management of such cases.

The *classification of gastric diseases* is in a transitional state at present. As a rule, textbooks enumerate two groups of diseases, one group the classification of which is based on anatomical findings (gastritis, ulcer, carcinoma, syphilis, etc.), and another group which represents the different abnormalities of the gastric function (disorders of secretion, of motility, of sensibility, etc.). In most textbooks the latter group is discussed under the heading of neuroses. This is erroneous, for functional disturbance is not at all identical with nervous disturbance, as is so often claimed. While, in a certain number of instances, disorders of gastric function are mainly due to a derangement of innervation, yet in the majority of cases they are connected with organic changes, and form merely the very earliest symptoms of the very gastric diseases mentioned with the first group.

The different varieties of disturbed gastric function merit separate discussion, because not only in neuroses, but also in organic diseases, disorders of the gastric function are the dominant feature of the clinical

picture. In both types of disease a well-arranged treatment should set out to correct the disturbance of function, which is usually th cause of subjective suffering and frequently gives rise to the development of anatomical alterations.

In order to establish a better classification of gastric diseases than that heretofore in use, the reviser of these lines has endeavored to give what both author and reviser consider a more exact form of classification, answering both scientific and practical purposes, which is now for the first time arranged and set forth in this book.

In the chapter on Organic Diseases, the reviser has given a new grouping to diseases of the stomach, making it more in accordance with the classifications usually employed in handbooks of pathological anatomy —an arrangement which he has not seen used in any work on Stomach Diseases. The principal grouping of gastric disorders into primary and secondary should serve to eliminate a good deal of the confusion still existing in regard to the classification of certain types. According to this classification, all the *true* gastric diseases are placed in the first group, while the secondary gastric disorders encountered in heterogeneous affections, in which the gastric phenomena are of symptomatic value only, are briefly summed up and discussed in a special chapter. A glance at the table will make the classification clear.

Classification of Stomach Diseases

I. Primary diseases of the stomach
  A. Organic diseases
    1. Genuine local gastric diseases
      a. Congenital defects, malformations, abnormalities
      b. Catarrh
        (1) Acute; food poisoning
        (2) Chronic
      c. Amyxorrhea gastrica
      d. Regressive processes, degenerations
      e. Necrosis (chemical poisonings)
      f. Tumors
        (1) Malignant
          (a) Carcinoma
          (b) Sarcoma
        (2) Benign
      g. Pseudotumors (foreign bodies)
    2. General diseases, localized in the stomach
      a. Lues
      b. Tuberculosis
    3. Constitutional diseases with organic lesion
      a. Ulcer

B. Constitutional diseases
1. With anatomical lesion—ulcer (same as A, 3)
2. Without anatomical lesion

a. Functional Disturbances

Secretory	*Motor*
Irritative	Without motor insufficiency
Hyperacidity	Constant disorders
Hypersecretion	Atony
Alimentaris	Ptosis
Continua	Temporary disorders
	Spasms
Depressory	Vomitus, etc.
Achylia gastrica	With motor insufficiency
Anaciditas	Acute
Hypaciditas	Chronic

b. Neurosis Ventriculi

(as a constitutional disease without anatomical lesion and without functional disturbance)

(1) Hyperasthesia
(2) Bulimia, etc.

II. Secondary diseases of the stomach detailed in 7 groups (see page 631).

The reviser wishes to emphasize the importance of the constitutional factor in dealing with the different forms of functional and neurotic disturbance and the possibility of the successful employment of general treatment and uniform therapeutic procedures, even in the seemingly contrary forms which these gastric neuroses with their kaleidoscopic manifestations so frequently assume.

He has endeavored to abate in some measure the confusion in the classification of the functional diseases, applying the term "functional disorders" only to those cases in which functional disturbance of a secretory or motor character is present, restricting the term "neurosis" to cases where sensory disturbance alone exists, discriminating between visible, controllable alterations of secretion or motor function, on the one hand, and sensory disturbances—often wholly independent of coexisting functional disorders—on the other.

He believes that the need of such a classification will be appreciated as soon as one realizes that when we talk about sensory disturbances we are, strictly speaking, talking about something that does not exist at all as when we speak of disturbances or disorders of an existing function—for example, in the case of secretory or motor functions, when either a depressory or irritative change in the function takes place. But as under normal conditions—save for the physiological sensations of hunger and satiety—the stomach has no sensations, neither can alterations in this "non-existing" function be supposed so that all kinds of sensory

manifestations have only the significance of a neurosis. In the true neurosis there are no anatomical alterations whatsoever; while in the functional disorder some slight alterations may be observable though often only by the aid of a microscope; such changes have been observed in achylia gastrica and glandular atrophy, in hyperchlorhydria with proliferation of the glandular tissue and when spastic conditions induce thickening of the muscular wall or the occurrence of spasms induces changes in shape and configuration.

A special chapter has been devoted to the employment of the X-ray in the study of gastric diseases because he feels that the practical and scientific significance of this aid to diagnosis is now so universally appreciated that a brief summary of our present knowledge of it might prove acceptable.

Regarding the treatment of incurable cancer, he has endeavored only to give a general outline, accentuating the difficulties which unfortunately we are forced to encounter in all diseases in which no therapy is of any avail, one of the most difficult situations in which the physician can be placed.

New material has been introduced, notably that on Amyxorrhea Gastrica, Gastric Tuberculosis, Sarcoma and Benign Tumors, Intoxications, Degenerations, etc., and an enumeration and brief description of the different forms of motor and sensory disturbance has been added. This work is concluded by the new section on Secondary Diseases of the Stomach for it seems superfluous to add that all the drugs mentioned and the therapeutic measures advocated are in accordance with the most recent authoritative practice along these lines.

PRIMARY DISEASES OF THE STOMACH

(*Organic Diseases*)

Congenital Defects, Malformations and Abnormalities

By congenital defects, malformations and abnormalities are indicated pathological conditions, such as congenital stenosis or atresia pylori, abnormally large or small size of the viscus, transposed position, hourglass stomach, etc. The treatment of such conditions, if any alleviation is possible, belongs in the domain of surgery.

Acute Gastritis

Various classifications have been made in regard to different forms of acute gastritis. The principal forms are: (1) the simple acute gastritis, usually caused by errors in diet; (2) the secondary acute gastritis, accom-

panying a great number of acute infections and febrile diseases; (3) the so-called toxic gastritis, following the ingestion of exogenous poisonous substances; (4) the phlegmonous gastritis.

We are dealing here in this chapter mainly with the first form of simple acute gastritis, which occurs as an original primary disease.

The discussion of *secondary gastritis* belongs in the general section on secondary gastric diseases. The *phlegmonous form* is discussed in surgical textbooks. *Chemical poisoning* is dealt with in the section on Necrosis. Primary, *toxic gastritis* which is caused by *bacterial food poisoning* and *botulism* is a very important subject in the general practice of medicine and is deserving of a brief separate discussion.

Simple Acute Gastritis.—The treatment of simple gastritis must, in the first place, be prophylactic in all persons who are predisposed to the disorder and have had repeated attacks of it. They should avoid all the injurious influences which may affect the stomach from within and from without: excessive indulgence in food and the overloading of the stomach with plain and, still more, with heavy and indigestible substances; exposure to rapid changes of temperature with insufficient protection of the body; fatigue and undue excitement. Especially such patients as have enfeebled digestive organs should exercise discretion and avoid all these possible harmful influences.

The causes for acute gastritis vary greatly. With some people the taking of a different water is sufficient to bring on an attack. Every person susceptible to such disturbances should learn to avoid what is most harmful in his individual case.

In treating the attack itself we should keep in mind that acute gastritis undergoes spontaneous cure by the operation of two natural factors, namely, the evacuation of the stomach by vomiting and the period of rest which is imposed upon the organ by the suppression of appetite. In the majority of cases it is sufficient not to disturb the activity of these two factors.

When we find that the stomach still contains noxious material we should support the natural tendency of the organism and assist the stomach to rid itself of irritating contents. If emesis does not occur spontaneously it is the custom of many physicians to bring it about. With some patients the drinking of hot water or the tickling of the palate suffices. Some practitioners favor the administration of *emetics,* either given by mouth [20 gr. (1.3 gm.) of powdered ipecacuanha, followed in a few minutes by a tumblerful of hot water], or hypodermically in the form of ¼ gr. (0.016 gm.) of apomorphin. All substances like mustard, sulphate of copper, tartar emetic, which cause vomiting by direct irritation of the gastric mucosa, must be avoided, as they tend to increase the existing inflammation.

But even the more rational emetics (ipecac and apomorphin) should

be used very reluctantly and only in case of great urgency, because all emetics have the great drawback that they produce a very depressing effect on some individuals and, furthermore, that vomiting, no matter in what way brought about, never completely removes the stagnating and irritating gastric contents.

Gastric Lavage.—All these disadvantages are avoided when, instead of employing emetics, we make use of the most effective means of thoroughly evacuating the stomach, namely, gastric lavage. The flushing of the stomach with plenty of warm water (containing some bicarbonate of soda) not only removes remnants of food, but also the thick and tenacious mucus which usually sticks to the mucosa and is a constant source of irritation, causing nausea, retching, and repeated vomiting, even after all food has been removed from the stomach. No other form of treatment subdues all these symptoms more quickly than lavage, and we should employ this most excellent remedy in all cases where persistent nausea or recurring vomiting of small quantities of mucus indicates the presence of irritating contents.

Repeated vomiting may prove very exhausting; therefore we should not readily dispense with this most effective method, persuading, if necessary, the patient to give up his prejudice to the procedure. The cleansing with plain (weakly alkaline) water may be followed by washing with a mild antiseptic solution when feasible. Hemmeter recommends for this purpose: Thymol, 7 gr. (0.5 gm.), boric acid, 4 dr. (16.0 gm.), water, 1 pt. (500.0 gm.).

Evacuation of the Bowels.—The cleansing of the stomach should be followed by a thorough evacuation of the bowels. In trying to rid itself of its irritating contents the stomach expels some into the intestines, where they undergo fermentation, the products of which provoke diarrhea and frequently are the cause of continued gastric irritation and vomiting, only ceasing when the putrefying intestinal contents are removed. Energetic purgation has always been considered essential in the treatment of acute gastritis. Purgatives, however, should not be given before we are convinced that the stomach is empty in order to avoid forcing more fermenting gastric contents into the bowels. We should further avoid undue irritation by not giving cathartics which the patient knows will cause irritation of the stomach.

Ordinarily castor oil is considered the most efficient drug; others prefer calomel, which is said to act directly as a gastric sedative in cases with persistent nausea and vomiting. Calomel is given in single doses of from 0.2 to 0.32 gm. (3 to 5 gr.), or in doses of 0.016 to 0.03 gm. (¼ to ½ gr.), repeated every hour until purgation takes place. In either case it should be followed by a saline cathartic, seidlitz powder, sulphate of sodium or magnesium, etc. Some authors prefer saline cathartics altogether.

The removal of the intestinal contents may also be effectually accomplished by thorough colon irrigations which follow the purgation by

mouth or take its place when great irritability of the stomach makes it advisable to avoid purgatives. Colon irrigations are often of great assistance when used correctly at the beginning of the attack before the purgatives begin to act.

When nausea and retching persist, or when pyrosis is annoying, alkaline powders are indicated, and usually relieve the symptoms. Various mixtures may be made up by combining either magnesia or bismuth preparations with bicarbonate of soda, adding some resorcin or menthol preparations.

Alleviation of Pain.—Abdominal pain is best alleviated by the application of hot-water bags, hot poultices, turpentine stupes, or alcohol compresses. In febrile cases cold compresses or the ice-bag is preferred. The pain is rarely so intense that it requires the hypodermic administration of morphin, 0.016 gm. (¼ gr.), and 0.0005 gm. (1/50 gr.) of atropin. Since morphin is liable to increase the tendency to vomiting, ext. opii, 0.03 to 0.05 gm. (½ to ¾ gr.), in suppositories, or codein, also preferably in suppositories, 0.05 gm. (¾ gr.) per dose, is more suitable in such cases, the dose to be repeated several times if necessary. Aside from this all medication should be omitted.

Diet.—The very important indication of putting the stomach completely at rest and thus giving the inflamed organ a chance to return to its normal condition necessitates total abstinence from food. A starvation period of one or two days is curative in these cases, and the more strictly the rule is observed the quicker the recovery. Even fluids should, if possible, be avoided. When thirst is very excessive cracked ice may be given in small quantities. In many cases small quantities of hot water are better tolerated and at the same time serve as an internal lavage.

With great exhaustion it may be necessary to add some champagne to the ice pills or some brandy and carbonated water in small quantities. It may further be advisable to supply some fluid and nutritive material by enemata consisting of saline solution and glucose.

After one or two days, according to the severity of the case, nourishment by mouth may be resumed. At first only fluids in small quantities should be allowed. When milk is tolerated it is a very suitable food, and is best given diluted with carbonated water; in other cases gruels, mutton broth, bouillon, or weak tea is preferable. In further enlarging the diet list preference should be given to soft, starchy foods. For several days the rule should be observed to have all food mechanically well prepared and free from fibrous and stringy parts, on the whole following the dietetic rules given in the section on Depressive Secretory Disorders. Patients who are subject to attacks of acute gastritis should proceed slowly in returning to ordinary diet, in order to prevent the development of subacute or chronic gastritis. They should abstain from taking coarse food for several weeks.

If, after the acute attack, symptoms of gastric irritation (soreness, pyrosis, etc.) continue, alkaline powders or an alkaline water (Vichy) may be of great aid and may be continued with benefit for several weeks.

In other cases with failing appetite and protracted weakness hydrochloric acid is of greater service. Not infrequently, however, hydrochloric acid, when given on an empty stomach, provokes pain by irritating the hypersensitive mucous membrane and should therefore be given well diluted and after meals. Before meals we give tinct. nucis vomicæ (5 to 15 drops) or some of the bitters; tinct. aurantii, tinct. gentiani. comp., tinct. cinchona comp., fluid extract of condurango, of each from 15 to 25 drops.

As a general rule, however, it is better to abstain from overstimulating gastric activity, but to allow the stomach to rest and so return unaided to its normal condition.

Toxic Gastritis

(*Bacterial Food Poisoning or Ptomain Poisoning*)

Ptomain poisoning is a special form of toxic gastritis or gastro-enteritis. It was formerly taught that food poisoning was due to the presence in the ingesta of alkaloidal substances called ptomains, which might alone, without bacterial action, cause intense intoxication. Now we know (W. H. Willkox) that ptomain poisoning is due to intoxication by food contaminated with bacteria. The source of contamination is to be found in insanitary conditions of preparation (slaughtering, cutting-up process, mincing, etc.) or of the storage of such foods as meat, sausage, fish or canned foodstuffs.

The assumption that extremely severe forms of acute gastro-enteritis are produced, not so much by the ptomain substances present in foodstuffs as by bacterial action, is favored by the observations of Galambos who found, contrary to the earlier views (Schottmueller, Jochmann), that these peracute forms of gastro-enteritis were, according to epidemiological experiences made during the World War, not observed in the form of large outbreaks, brought about by food poisoning, but appeared rather after the manner of contact infections in the diseases of bacteriemic origin, that is, in sporadic form. Bainbridge demonstrated, that the B. enteritidis aertrycke, identical with the B. suipestifer, plays the most important etiologic rôle; second in importance is B. enteritidis Gärtneri; among different bacteria productive of ptomain poisoning, B. paratyphosus A should be mentioned in this connection. Galambos observed in a patient convalescing from a severe bacteriemic paratyphoid A infection, a sudden fatal onset of gastro-enteritis acuta paratyphosa A with clinical symptoms very like those of cholera; postmortem examination

showed anatomical pathologic alterations which resembled those found in cases of dysentery.

A special form of food poisoning is produced by B. botulinus, the condition called "botulism." Either the bacteria or its toxins may produce the clinical picture of botulism. The toxins resemble those of diphtheria and tetanus, having a special affinity for the nerves, and its antitoxin has a pronounced therapeutic effect when administered early enough.

In food poisoning the entire gastro-intestinal tract will show signs of a severe, often hemorrhagic inflammation.

In the treatment of botulism, in addition to the principles laid down for simple gastritis, colon irrigation, hypodermic and intravenous application of isotonic and hypertonic NaCl solution may be used.

Chronic Gastritis

The term chronic gastritis, formerly much abused and applied to the most varied gastric disorders, comprises only cases in which gastric analysis demonstrates an increased secretion of mucus usually carrying cellular elements as a sign of anatomical alterations of the mucosa. The secretion of hydrochloric acid is diminished or absent.

Chronic Mucous Gastritis.—In a certain group of these cases during an earlier stage the increase of mucus is associated with hyperacidity and hypersecretion (acid gastritis). The treatment of this special form is discussed under irritative gastric disorders. It is frequently observed in alcoholics and, although in some of these cases the irritative secretory disorder may remain unchanged during many years, there is a tendency in others to develop into mucous gastritis, the secretion of acid and ferments gradually diminishing with a progressive destruction of the peptic glands until finally complete atrophy of the glandular mucosa is established. This state of chronic atrophic gastritis is also observed in non-alcoholic forms of chronic mucous gastritis. When this state is reached it presents principally complete lack of gastric secretion. The treatment of this condition is discussed under Achylia Gastrica.

We are then dealing here with the treatment of chronic mucous gastritis only.

Primary and Secondary Chronic Gastritis.—It is customary to distinguish between primary and secondary chronic gastritis. While for purposes of description the separation into primary and secondary forms may be practical, yet we should remember that in many cases of so-called secondary chronic gastritis the same harmful influence which causes the disease of the remote organ also provokes a primary gastritis by direct deleterious action on the stomach, so that we have a combination of primary and secondary gastritis, for instance, in alcoholic affections of the heart, liver, and kidneys, in gout, diabetes, chronic nephritis, etc. This shows the necessity for treating many cases of secondary gastritis

not only indirectly by attending to the disease of any other organ which is one causative factor in its development, but also by dealing directly with the diseased stomach.

For both forms, primary and secondary gastritis, we have to consider first of all the causative treatment, which means at the same time the best method of prophylaxis when undertaken during the earlier stages of development.

We should eliminate, if possible, the causative factor which has caused the disease: constant abuse of alcohol is responsible for the majority of cases; next to alcohol ranges tobacco, both when smoked (particularly when inhaled) and when chewed. The individual tolerance for these toxic substances varies greatly; a quantity which acts deleteriously with one person is harmless for another. The same feature of different individual tolerance will be observed in regard to other direct causes of chronic gastritis; habitual overindulgence in highly seasoned and rich courses, frequent overloading of the stomach with indigestible and fermentable articles of food, hurried eating and bolting of poorly masticated food, especially when meals are taken while under high mental pressure or during periods of great excitement; abuse of iced water and iced drinks of different kinds, so common in this country; habitual or long-continued use of drugs (iodids, salicylates, quinin, mercury, arsenic, silver, cubebs, sandalwood, etc.). We must mention as a very frequent cause the abuse of purgatives, in particular of concentrated saline cathartics which we have found as a causative factor in a high percentage of our cases. In another group we have to put the blame on overindulgence in strong tea or coffee. All these causes prove particularly harmful in people who are predisposed on account of anemia or when general weakness and neurasthenia lessen their power of resistance. Among the direct causes of chronic gastritis we further count diseases of the teeth and gums, which act by the harmful influence of swallowed products of decay and pus and not less so by preventing proper mastication.

Secondary Chronic Gastritis.—In secondary chronic gastritis the treatment of the primary disease is of the utmost importance and should always be combined with the direct treatment of the gastric disorder.

Chronic gastritis is frequently associated with other diseases of the stomach, as cancer, the latter stages of peptic ulcer, motor disorders, displacement of the organ, especially by the effect of adhesions, etc. In arranging a plan of treatment we have to take these factors into account.

The most frequent occurrence of secondary gastritis is observed in all diseases which lead to chronic venous congestion of the stomach by disturbances of circulation, diseases of the heart, the lungs, and the liver. The direct treatment of these diseases often proves the best means of combating chronic gastritis as, with improvement of circulation, the state of engorgement of the gastric mucosa is removed or diminished.

Thus we understand the very beneficial effect which often follows the use of digitalis, even when this drug temporarily aggravates the gastric condition. In such cases the hypodermic administration of modern digitalis preparations is preferable and of great value. Great improvement follows the action of digitalis and other heart tonics in those cases of secondary gastritis which are caused by chronic nephritis.

The treatment of the underlying cause plays a great rôle in all cases where chronic gastritis is secondary to metabolic derangements as the uric acid diathesis, gout, diabetes, to diseases of the urinary tract, or to chronic infectious diseases. We must particularly mention here tuberculosis, in which the symptoms of chronic gastritis are often so prominent that in incipient cases they completely overshadow the primary disease. While the proper attention to the gastric disorder will invariably assist us in improving the state of nutrition great care should be used to avoid in such cases a diet which leads to underfeeding of the patient. On the other hand, in such cases we should be very careful with forced feeding, which, as a rule, is indiscriminately recommended for all tuberculous patients. We have frequently seen disregard of an existing gastritis greatly aggravate the digestive disturbance and so lead to dismal failure of the attempt to improve the general nutrition.

The consideration of the causative factors should always be combined with the direct treatment of the diseased stomach in secondary as much as in primary gastritis. Too often the physician is satisfied with directing all attention to the treatment of the primary disease of the heart, the lungs, the kidney, etc. It should be expressly stated that in improving the condition of the stomach by direct treatment we greatly assist the causative treatment of the underlying disease.

Gastric Lavage.—The treatment *par excellence* is gastric lavage. Its advantages are many. It answers the most important indication of removing the mucus, which when adherent to the mucosa prevents its secretory activity and, when mixed with the ingesta, prohibits the intimate contact of gastric juice and food. Lavage further directly stimulates the sluggish gastric secretion and improves the state of the mucosa, by promoting its circulation. The beneficial action of lavage can be greatly enhanced by the use of different solutions. Mucus is not very soluble in ordinary water. We have to add 1 teaspoonful of bicarbonate of soda to a quart of warm water, or 1 teaspoonful of a mixture corresponding to the ingredients of the water of Ems (2 parts sodium chlorid and 1 part sodium bicarbonate). Mucus is more effectually removed when lavage is given under high pressure. After washing two or three times with such solutions, J. Kaufmann often employs limewater with very good results (1 part of limewater diluted with 1 to 4 parts of distilled water; total amount of mixture, 300 c.c.). Limewater acts as a solvent of mucus and as an astringent. Harnack states that it is the only drug which combines

both qualities. Solutions of sodium bicarbonate and of sodium chlorid merely dissolve the mucus. Other astringents, instead of dissolving, coagulate mucus. Limewater has the great advantage of first dissolving the layer of mucus and then reaching the deeper layers of the mucosa and acting as an astringent.

When the amount of mucus is not excessive dilute solutions of zinc sulphate are useful as astringents (1:5,000, gradually increased to 1:1,000). The application of *silver nitrate* (in similar solutions) is recommended in cases which show gastric hyperesthesia and frequent pain. Some authors attribute the pain to the presence of erosions and ulcerations, which develop in certain cases of chronic mucous gastritis (ulcerative chronic gastritis). The great vulnerability of the mucous membrane in chronic gastritis is often manifested by the appearance in the wash water of small pieces of mucous membrane detached by the traumatic effect of the tube. There is no justification for basing on the finding of these fragments of mucosa a special form of gastritis (erosions—Einhorn; gastritis exfoliativa).

When chronic gastritis is associated with motor disorders lavage is especially indicated for removing stagnating and fermenting masses. In such cases we may use for final lavage antiseptic solutions: salicylic acid 1:1,000; boric acid 5:1,000; resorcin 2:1,000; thymol 1:2,000; hydrochloric acid 5:1,000. The removal of irritating substances is further an indication for lavage in chronic nephritis, when the stomach eliminates urea and other products of metabolism. We have frequently observed great improvement result from gastric lavage, when the presence of these substances in the stomach caused persistent nausea, vomiting, foul tongue, etc. There are many other conditions in which the stomach serves as an *excretory* organ and where the excreted substances are the cause of gastric irritation and of chronic gastritis. In all such conditions lavage is an excellent form of treatment. When lack of appetite is a prominent feature we use weak solutions of hops, quassia, and other bitters for final lavage, of which some may be left in the stomach. The modern beers of low alcohol content may be useful.

The frequency of lavage depends on the severity of the case and on the progress effected by the treatment. When much mucus is formed, and particularly when stagnation of food is present, daily lavage is indicated and best performed in the morning, when it prepares the stomach for the day's activity. In cases of severe character with stagnation and pronounced fermentation it may be advisable to perform lavage before the evening meal; or both on a fasting stomach and in the evening. We diminish the frequency of the treatments with symptoms of improvement, giving lavage every other day, then every third day, and finally once a week. In many cases the improvement which follows lavage sets in remarkably soon after a few applications, manifested by the greatly dimin-

ished amount of mucus, the lessened discomfort, the increased appetite, and other signs of improved gastric activity.

The drinking of suitable natural and artificial mineral waters is often described as internal lavage. Its effect is increased when the patient, after drinking the water, rolls around to get the water thoroughly in contact with the stomach wall. Even used in this way it is only a poor substitute for lavage by means of the tube. Still the drinking of these waters is helpful and should be recommended for days when no lavage is given and after lavage is stopped altogether. They may be taken for long periods of time. Considering the diminished state of secretion the sodium chlorid waters are indicated as described under Depressive Secretory Disorders, to which we here refer. Under this heading will also be found the rules for regulating the diet and for medication, which, with chronic gastritis, are essentially those given for depressive secretory disorders in general.

We wish to point out here the great importance of regulating the activity of the bowels. In many instances the chronic gastritis proves intractable as long as intestinal disturbances prevail. Under the heading Depressive Secretory Disorders we described the diet which is indicated when diarrhea is present, avoiding in the first place all albuminous food, which is liable to undergo intestinal putrefaction. The effect of proper dieting can be greatly supported by systematic colon irrigations, which prove of high value particularly at the beginning of the treatment in thoroughly removing all putrefying intestinal contents.

Constipation should be treated dietetically by increasing the amount of well-prepared vegetables and stewed fruits, by adding honey or milk-sugar to breakfast foods, by giving buttermilk, sour milk, and other fermented milks. If not efficient, enemata, colon irrigations, or oil enemata are in place. Cathartics per os should be omitted. When they cannot be avoided the very mildest are indicated, preferably small doses of vegetable cathartics, cascara, rhubarb, etc. Strong saline cathartics are permitted only when chronic gastritis is associated with a state of pronounced abdominal plethora (congestion and cirrhosis of the liver, cardiac insufficiency with intense abdominal congestion). In all other cases strong saline cathartics only aggravate the inflammatory changes of the gastric mucosa and should be forbidden.

Very helpful in the treatment of chronic gastritis, especially when combined with constipation, are different methods of gymnastics, of general and abdominal massage, and of various electric and hydrotherapeutic measures. They are all applied with the intention of improving the circulatory conditions in the abdomen and its organs with the effect of raising the tonicity of the abdominal wall as well as of the stomach and intestines. They often accomplish this task when judiciously employed. Too frequently, however, these methods are overdone, with the result that

they lower instead of raise abdominal circulation and tonicity. The general advice given to patients to use one or the other or several of these methods is inadequate; there should be an exact dosage prescribed and regulated according to its effect.

Amyxorrhea Gastrica

To the section on Gastritis a short account of amyxorrhea gastrica (J. Kaufmann) should properly be added. While gastritis is characterized by an increase in mucus secretion, amyxorrhea—as its name indicates—presents a total absence of mucus, a condition which can be demonstrated by the microscope and even by the unaided eye. Amyxorrhea is a morbid condition which may exist either entirely without symptoms, to be recognized only by accident, or may be the origin of various complaints referable to the stomach which have been heretofore classified as gastric neuroses. No stomach trouble should be designated as a gastric neurosis until all other possibilities have been excluded; it should be always the diagnosis of last resort.

No doubt, in the light of further progress and the increased knowledge which may come to us in the future, even those conditions which are now named collectively as "gastric neuroses" may be differentiated, and clearly proved heterogeneous in character, representing separate disease entities. By Kaufmann's researches, one such condition—amyxorrhea—has already been segregated. This affection can be present in a stomach otherwise healthy, or it can be coexistent with secretory disorders. Evidences of hyperacidity can often be traced to this cause alone, because there is no stratum of mucus to protect the stomach lining from the excessive chemical action of hydrochloric acid, the physical effects of heat and cold, etc. The absence of mucus likewise exposes the mucous membrane to injury, which may result in hemorrhagic erosions and ulcer.

Kaufmann strongly advocates the use of silver nitrate solutions for stimulating the secretion of mucus. Lavage with silver nitrate solution (1:1,000 to 1:5,000) will cause an outpouring of mucus, thus bringing about a practical cure of conditions of amyxorrhea or of pseudohyperacidity due to lack of mucus, even when after treatment an unchanged high concentration of hydrochloric acid proves that symptoms disappear with the abolition of amyxorrhea, even when hyperchlorhydria persists.

Regressive Alterations: Degenerations

Degenerations of the gastric mucosa are often secondary localizations of a generalized process. According to Ribbert the following regressive alterations can occasionally be observed:

1. Fatty degeneration, subsequent to poisoning with phosphorus and arsenic.
2. Amyloid degeneration, as a special localization of the general amyloidosis.
3. Calcium salt incrustation and deposition, in processes of bone resorption.
4. Gastromalacia which, if a partial process, may predispose to ulcer.

From the therapeutic standpoint these conditions do not call for special attention; the underlying cause should be sought and the treatment, if any is possible, should be directed against it.

Gastric Necrosis from Chemical Poisonings

Poisonous substances which reach the stomach can cause a severe deep-seated inflammation, or even necrosis. Milder cases can be classified as toxic gastritis under Acute Gastritis, but the more severe forms requiring special description can be placed under the heading of Necrosis, which is reserved for them. The same pathological process which takes place in the stomach occurs in the mouth, esophagus, and intestines, the condition in the mouth indicating the character and intensity of the corrosive effect in the stomach. The entire stomach lining may be affected, or the corrosion may act only upon isolated areas of tissue, especially on the top of the rugæ produced by the contraction of the musculature.

The therapy of necrosis has two aims: (1) the removal of the poison; and (2) the administration of antidotes. For the first we must resort to lavage of the stomach and also of the intestines, but if a rubber tube is applied the danger of perforation must be kept in mind, especially in severe forms of necrosis when tumefaction or liquefaction of the mucous membrane is suspected, and it must be used with extreme caution if at all.

According to Bassler, among the antidotes to be employed are, "in the caustic alkalis, dilute vegetable acids, lemon and lime juice, or vinegar; in antimony, tannin in demulcent drinks; in arsenic, sesquioxid of iron, made by adding carbonate of sodium to tincture of the perchlorid, or dialyzed iron may be used; in carbolic acid, alcohol, solution of sulphate of magnesia or of soda, dilute sulphuric acid or saccharated solution of lime; for hydrocyanic acid, 2 drams of magnesia in water, followed by 15 minims of perchlorid of iron and 12 gr. of ferrous sulphate in aqueous solution; in iodin, starch water; in mercurial salts, white of egg and flour; in oxalic acid, lime or magnesia; in phosphorus, sulphate of magnesia. The use of olive oil or molten vaselin in the stomach after neutralization and lavage diminishes the effect of the corrosive poisons, excepting in phosphorus poisoning. . . . Additional matters of treatment are the use of morphin to control the pain and general distress, bismuth and bits of ice to allay

the irritation, and an ice-bag externally in cases of peritonitis. Nutrition should be maintained by rectal enemata only; and resource to stomach feeding should not be permitted until recovery is well established."

NEW GROWTHS OF THE STOMACH

Carcinoma Ventriculi

Cancer of the stomach is a surgical disease and the discussion of its treatment principally belongs to textbooks on surgery. However, in clinical practice, gastric cancer is usually treated by the internist, not only in its earlier stage (when it is often called a "gastric neurosis" or "catarrh of the stomach," almost up to the time of operation), but also after operation, when the patient has been dismissed from the surgeon's care. This refers to the operable cases. In those which are inoperable the internist usually attends the case from beginning to end. And so, although the malady itself is a surgical disease, its clinical care falls into the internist's hands, in every instance, with an exception of the eight or ten days immediately after operation.

Treatment.—The treatment of gastric cancer requires radical extirpation of the tumor, together with an extensive resection of all the regional lymphatic glands. When radical operation is not feasible—on account of metastases or inoperability of the tumor—when motor insufficiency with stagnation is present, if the condition of the patient does not contra-indicate such a procedure, palliative gastro-enterostomy should be done.

In the earlier stage of the disease the physician's main task is to establish an early diagnosis, that is, to discover the necessity of immediate surgical intervention; later, if the case proves to be inoperable, to hide from the patient the hopelessness of his condition and to make liberal use of symptomatic treatment.

The establishment of an early diagnosis requires all the knowledge and skill of the physician and the employment of every help available as a diagnostic aid. For this reason a brief discussion of the chief means of diagnosis can appropriately be placed here.

In the establishment of an early diagnosis, beside the history, the findings of the functional tests and the results of the X-ray examination are of the highest importance; but the most reliable information can be gained—in case of a palpable tumor—by a careful, thorough physical examination.

In the *history,* the most important data are:

1. The age of the patient (between 40 and 60 years or over).
2. The relatively short duration of the disease (weeks or months) and

often the abrupt onset of symptoms in patients who have never previously suffered from gastric disturbance.

3. Comparatively marked loss of weight and strength.
4. Anemia and beginning cachexia.

Pain, undefined gastric complaints, aversion to special kinds of food, particularly meat, are of less significance.

Signs of motor insufficiency, the vomiting of "coffee-ground" material and tarry stools are highly significant, but are not early symptoms.

Frequently, in incipient cases, *physical examination* does not reveal anything, the tumor becoming palpable only when the disease is more advanced. When located at the pylorus, in contradistinction to benign pyloric stenosis, stiffening of the stomach with the concomitant "Spritzgeraüsch" is rarely found.

The palpability and size of a tumor alone cannot decide the question of operability, because a tumor easily accessible to the palpating hand may still be removable, while in other cases, although no tumor is either visible or palpable, operation will reveal a growth already too far advanced for removal to be possible.

Functional examination will in most cases reveal anacidity and motor insufficiency with stagnation. The total acidity is often relatively high, due to the presence of organic acids, especially their main representative lactic acid. The presence of these organic acids is the result of achlorhydria *plus* motor insufficiency. When either one is absent no lactic acid will be found. The long bacillus of Oppler and Boas has only a relative value; it represents but one type of lactic-acid-producing bacteria.

X-ray examination shows filling defect, with typically uneven and irregular edges and surface, and a lack of peristalsis on the site where the growth is located. If it is at the pylorus, signs of gastric dilation, six-hour residue, and sometimes hyperperistalsis as well as reverse peristalsis may be present; while, in cases of infiltrating tumors (scirrhus), shrinkage of the involved part of the viscus is a usual finding.

In addition to all these means of diagnosis *gastroscopy* should be mentioned, but in our opinion even an exploratory laparotomy is less harmful, less dangerous and will give more reliable results than an exhausting gastroscopic examination. Maelpe who used Elsner's gastroscope in 500 cases of different pathological processes could establish an unquestionable diagnosis in but 13 cases out of 17 where gastric cancer was present, a percentage no higher than that obtained by more simple, less painful and less trying methods of examination.

When the diagnosis of cancer has been established, or even if a strong suspicion of its presence can be aroused by certain findings, operation should be undertaken.

We must operate at an earlier date and in order to accomplish this we would speak very emphatically in favor of exploratory laparotomy when the suspicion of a developing cancer is sufficiently substantiated by some objective findings and before a positive diagnosis is made by the palpation of a distinct tumor. We are far from advocating laparotomy in every case presenting persistent dyspepsia and malnutrition. The suspicion of a gastric cancer must be based upon some objective finding, which often could be had if only looked for. This is not the place to discuss the early diagnosis of gastric cancer. It is, however, not superfluous to state that in the majority of cancer cases which have come to our personal knowledge no previous examination of stomach contents had been performed, although the whole course of the case must have suggested the possibility of a cancerous growth for many months.

Unfortunately surgical removal of gastric cancer does not always prove successful, and sooner or later metastases will occur. In other cases exploratory laparotomy will reveal that metastases are already present or the tumor may prove otherwise inoperable.

But even when operation is carried out in time, unsatisfactory results are not infrequently obtained, as is evidenced by the most recent statistics. For instance, James Ewing, in his work on *Neoplastic Diseases* (1922) states that resection itself exacts a high mortality, which is, in the hands of the best surgeons, such as Mayo, not less than 13 per cent (reduced in the last series to 7 per cent), or 17.7 per cent (Kocher). Other surgeons operate with still higher mortality. Three years after operation, final healing could, according to H. G. Paterson, be observed in only 8 per cent, and in Mayo's statistics, in 20 per cent (in the last series 37.6 per cent) of the operated patients. The majority of the cured cases might have been carcinomatous ulcers and adenocarcinomas (Kocher). Peck, in giving a survey of the hospital results in New York, states that among 480 operated cases 98 radical operations were performed, with an operative mortality of 28 per cent (143 exploratory laparotomies, 167 gastro-enterostomies). After from three to four years only eight were known to be alive. Friedenwald reports 1,000 cases, in 266 of which operation was performed. After eighteen months only 1 patient was still alive, all the others having died of the disease.

The *management* of the *inoperable cancer* is a very hard task. The more intelligent the patient, the harder is the task, especially if the patient be a member of a professional class, such as a physician, nurse, or midwife. Finding that the improvement promised before the operation does not afterward materialize; feeling that his strength is steadily failing and perhaps himself palpating the growing tumor, it becomes very difficult to hide the facts. Nevertheless, the truth should not be revealed by the physician. The attending physician's difficulties are increased when a patient with inoperable cancer becomes aware of the incurable nature of

his disease. The prescription of drugs is the easiest of the medical activities. It is much harder to keep up faith and hopefulness.

It often happens that, the patient losing confidence in his physician, with or without his regular attendant's consent, consults with others. Physicians called in under such circumstances should not reveal the truth to the patient himself, although it is wise that some relative or friend should be informed as to the true nature of the condition.

Regarding the question of *medicinal treatment* in inoperable cancer cases everything possible should be done, if only for temporary relief. Our first duty is to control pain as completely as possible. Bromids, chloral hydrate, antipyrin, aspirin, pyramidon, codein, dionin, papaverin, belladonna, atropin, pantopon, opium, and morphin are the principal drugs used for this purpose in the order of their strength and efficiency. They work best in combination. Later on, larger doses and stronger representatives of this series ought to be used. In severe pain, especially in institutional treatment, the anodynes may be administered hypodermically. There is no "maximum dose"; the amount prescribed is governed not by the rules of pharmacology, but by the severity of the pain present.

Morphin not only relieves pain, but it has the wonderful effect of deceiving the patient about his condition and thereby proves such a powerful help that the physician should never hesitate to administer it, even when gradually larger and larger doses are required. The probability that with a long-protracted course of the disease the patient may become a confirmed morphin fiend should not interfere with the liberal use of a drug which, in these cases, means a blessing for hopeless sufferers.

In order to increase appetite, we may give alternately bitter stomachics such as tinct. of china composita (Nanning), gentian, amara, Cort. aurantii, quassia, nux vomica, etc. When constipation is present, these may be combined with tinct. rhei (Darelli). Bitter teas taken before meals are sometimes a good adjuvant, and may be composed of herb. grandifolii galeopsidis, trifolii fibrini, lichenis islandici, marubii albi, etc. Condurango can be given in the form of decoctions with wine or fluid extract; sherry, whisky, liquors or sweet wines serve the same purpose. Although orexinum tannicum (as a remedy for anorexia) has been much praised we have seldom seen much, if any, result from it.

For the relief of other symptoms, accidentally present, such as constipation or diarrhea, anemia, debility, vertigo, etc., symptomatic treatment should be given as they arise.

Certain authors place high value upon the X-ray and radium in the treatment of gastric cancer administered both before and after operation, believing it to be efficacious in increasing immunity. Thomas R. Brown, however, maintains that he has seen no satisfactory result in any case of gastric cancer from the use of X-ray, or radium, or any of the various metals employed in colloid form.

Locally we can apply hot-water bags, flaxseed poultices, Winternitz's cooling apparatus, alcoholic compresses, etc.

Diet.—We must, in the first place, try to feed the patient properly, in order to keep up as long as possible his strength and the state of his nutrition. The arrangement of a diet, particularly in cases of prolonged duration, is often the most difficult part of the treatment. Complete lack of appetite and aversion to food may greatly tax the resources of the physician. We have to resort to advising all kinds of delicacies, to constant changes in the bill of fare, and must continually find other ways of preparing foods. In doing so we should always consult and follow the tendencies and even the whims of the patient rather than adhere strictly to a preconceived plan of dieting. Proceeding in this fashion we are often surprised to find certain foods, generally excluded from an invalid's diet, better tolerated than those recommended in such diet schemes. It is wise, however, to stipulate as a general rule that all food be mechanically well prepared and, if possible, finely divided so as to tax the activity of the stomach as little as possible and to facilitate its quick egress from the stomach. The selection of different types of food depends to a great extent on the state of gastric secretion. In cases which develop on the base of a chronic ulcer, acid hypersecretion often continues up to a very late stage of the cancerous growth. In such cases the diet should be arranged according to the rules given for irritative gastric disorders, permitting in particular the different kinds of lean meats, fish and poultry, milk, eggs, vegetable purées, etc. This kind of a mixed diet should further be advised in cases without hyperacidity as long as no aversion arises for meat and similar foods.

Aversion to meat and other animal food is frequently an early symptom of that type of carcinoma which is usually located at the fundus of the stomach, causes atrophy of the gastric peptic glands and complete lack of secretion. Here meat and similar food should be eliminated and a diet arranged conforming with the rules given in the chapter on Depressive Secretory Disorders, consisting principally of milk, farinaceous and starchy foods, purées of vegetables and of fruits, etc. Whatever type of food is chosen, it must be thoroughly prepared and should be presented in a palatable form. The individual meal should not be bulky and an interval of sufficient length should be allowed to facilitate the evacuation of the organ.

Lavage.—The most effective stimulus to appetite and gastric activity in general is gastric lavage, which, when properly handled, is by far the most valuable method of palliative treatment in gastric cancer. All the advantages which we described as going with gastric lavage when applied in cases of chronic gastritis, with irritative as well as with depressive secretory disorders, are observed in the same manner in cases of carcinoma. By removing stagnating and fermenting masses lavage re-

lieves discomfort, pain, and vomiting, it stimulates sluggish gastric secretion and increases the appetite, it facilitates the egress of chyme from the stomach, all of which greatly helps to raise the state of nutrition. Lavage proves beneficial further by removing toxic products of fermentation and putrefying masses from decaying tumors, often distinctly reducing the symptoms of severe auto-intoxication.

According to the type of fermentation we employ either alkaline or sodium chlorid solutions; we further make use of antiseptic solutions or of infusions of bitters when attempting to stimulate secretory activity. These methods of lavage are described in the sections on Irritative and Depressive Secretory Disorders.

The frequency of lavage depends on the degree of stagnation and on the severity of the subjective suffering. In most cases daily lavage of the fasting stomach is sufficient. Patients who are disturbed by pain and vomiting during the night are greatly relieved and secure sleep after evacuating the stomach late in the evening or during the night. In some cases we have to do lavage twice a day. Most of these patients learn to lavage themselves, and once they realize the great relief which follows it they insist upon its systematic application. Since no harm can be done the patient should be given a free hand in employing this valuable method of treatment. Not infrequently the effect of methodical lavage seems to go further than relieving suffering and improving nutrition. From my own experience I can endorse the statement of Fleiner, who observed a slower development of the cancerous growth in patients who systematically continued lavage for a long period of time.

Gastro-enterostomy.—Similarly we may meet with an arrest of cancerous growth after gastro-enterostomy. When pyloric obstruction is pronounced and symptoms of gastric dilatation continue to be annoying in spite of lavage and dietetic treatment, gastro-enterostomy should be performed, if feasible. The relief of symptoms after successful gastro-enterostomy is sometimes so marked, and the gain in weight so great, that doubt may arise regarding the correctness of the diagnosis. Still, however great the immediate result of gastro-enterostomy or methodical lavage may be, these palliative methods do not prevent the development of metastases, which usher in the final state of the condition.

Sarcoma Ventriculi

Cancer is the most common malignant growth of the stomach. In Bassler's opinion, however, sarcoma likewise is not a rare occurrence, and he suggests that, if systematic microscopical examinations were made, sarcoma might be revealed with much greater frequency among the so-called cancer cases than we have hitherto supposed. He bases this statement on the findings of C. Perry and L. Shaw, who discovered 4 sarcomas among 50

cases of malignant growths of the stomach (8 per cent) contrary to the general view and experience, which estimates this relation at about 1.5 per cent, or even as Stevens at 1 per cent.

In contradistinction to cancer, sarcoma can reach enormous size, develop at any age, more frequently in young adults (Stevens).

As to the treatment of sarcoma, the same principles prevail that were laid down in the chapter on Cancer.

Benign Growths

Benign tumors of the stomach are of rare occurrence. Leiomyoma, fibromyoma, lipoma, adenoma, etc., have occasionally been found. When a tumor has been diagnosed and its benignity recognized, which very rarely might happen, operation is imperative only in cases in which the growth, either by its size or its location upon the pylorus, seriously endangers the evacuation of the stomach; otherwise no operative therapy is desirable. In border-line cases, when tumor can either be palpated, or at least is strongly suggested, exploratory laparotomy should be performed.

Pseudotumors

Pseudotumors, gastroliths and foreign bodies, especially "hair balls" and accretions of fruit stones, both of which result from the swallowing of non-digestible substances, may grow to such a size that operative intervention is necessary. Foreign bodies of smaller size, swallowed professionally, accidentally or by the insane, can occasionally be removed perorally through the gastroscope (Jackson and Spencer).

GENERAL DISEASES LOCALIZED IN THE STOMACH

Syphilis of the Stomach

The Wassermann test will probably help to clear up the question whether syphilis of the stomach is rare, as Chiari's thorough anatomical investigations would indicate, or of frequent occurrence, as some authors (Neumann, Einhorn, and others) would have it, who base their claim on clinical data. The mere fact that the patient has had syphilis is certainly not sufficient to settle the diagnosis. In addition to the Wassermann test, X-ray findings can often confirm the diagnosis, or at least create a strong suspicion of the presence of gastric syphilis, which is one of the rarest of specific luetic lesions. According to Franklin W. White the roentgenologic findings are often very striking, but not especially distinctive. It is especially difficult to differentiate between leutic and can-

cerous manifestations. In making this distinction the following signs pointing to the diagnosis of lues ventriculi will be found useful (F. W. White): luetic subjects are often young and in fairly good general health; there will be a huge stomach lesion with a large filling defect and a tendency to hour-glass shape, but without a palpable tumor, or a six-hour residue; the Wassermann test will be positive and antiluetic treatment will result in changes in the gastric picture. For practical purposes, however, we do well to remember Hayem's proposition: always to think of syphilis when confronted with serious stomach trouble of obscure nature. The good results obtained in such cases by antiluetic treatment, after they had resisted all other forms of treatment, justify the application of antiluetic treatment not only when a positive diagnosis is made, but also when the suspicion is sufficiently corroborated. Aside from the specific treatment by arsphenamin, mercury, iodid, etc., the gastric disorder may call for special local treatment.

Syphilis of the stomach presents itself in the form of chronic gastritis, gastric ulcer, gumma, and fibrous-hyperplastic infiltration.

Chronic Gastritis.—According to Neumann, chronic gastritis is the most frequent manifestation of visceral syphilis, occurring during all the different stages of the disease. It differs symptomatically in no way from gastritis of other origin and should be treated along the same lines. When it is present the administration by mouth of antiluetic remedies, particularly of mercury, should be omitted. Great care should be exercised in prescribing iodids when hyperacidity is noted. The excess of hydrochloric acid, by freeing iodin, is liable to provoke iodism. It is therefore advisable to give iodids only when the stomach is free from acid contents and to administer them always in connection with large quantities of alkalis (bicarbonate of soda or magnesia preparations).

Gastric Ulcer.—Gastric ulcer of syphilitic origin shows identically the same symptomatology as an ulcer caused by other factors. While the general principles of treatment remain the same in every way for the syphilitic form as for others, yet the antiluetic treatment may be of paramount importance. Particularly in cases of uncontrollable gastric hemorrhage we should always think of a possible syphilitic origin. Fournier, Dieulafoy, and Hayem have reported cases of uncontrollable hemorrhage in which all other treatment failed and complete cure was established by giving mercury and iodids. *Perforation* calls for immediate surgical interference. With pyloric obstruction, however, a thorough antiluetic treatment should be instituted before proceeding to operate.

When the obstruction is caused by the inflammatory swelling of an active syphilitic ulcer the specific treatment may yield a complete cure.

Pyloric obstruction caused by the scar tissue of a healed ulcer requires surgical interference in syphilitic cases exactly as in others. The indication for operative treatment is also the same for syphilitic as for other

forms of indurated chronic ulcer of the fundus when it proves intractable to medical methods of treatment.

Gumma.—Gumma of the stomach is rarely diagnosed. When the tumor is palpated it arouses the suspicion of carcinoma. If a diagnosis of syphilis is made, or even with a well-supported suspicion, energetic antiluetic treatment is imperative. When the diagnosis is doubtful exploratory laparotomy and excision of a small piece may clear up the situation, as it did in a case reported by Lafleur, who found a gummatous ulcer causing an hour-glass stomach, and thereupon administered antisyphilitic remedies.

Pyloric obstruction caused by a gumma may be perfectly cured by antiluetic treatment. If the obstruction is pronounced and the patient greatly reduced in weight it may be advisable, according to Brunner's views and statistics, to perform gastro-enterostomy first and then follow it up with energetic antiluetic treatment.

Fibrous-hyperplastic Infiltration.—The same indication for surgical interference may turn up when Fournier's syphilitic fibrous-hyperplastic infiltration causes pyloric obstruction, as in cases published by Gross, Hemmeter-Stokes, and others. How far arsphenamine treatment will permit the postponement of surgical interference in pyloric obstruction of that and other types remains to be seen.

Gastric Tuberculosis

Gastric Tuberculosis.—Tuberculosis is only very rarely located in the stomach. Gastric tuberculosis usually occurs in conjunction with intestinal tuberculosis, but there are records of cases in which there was no focus of a tubercular process except the gastric one; therefore it can exist as an independent disease. The most frequent form is the tuberculous ulcer, which varies in size and number and is often located at the pylorus where it sometimes assumes the characteristics of an inflammatory pyloric tumor. In generalized miliary tuberculosis, the miliary tubercles may attack the gastric wall.

Two avenues of treatment lie open to us: (1) we may regard the pathologic anatomic substratum of gastric tuberculosis (as to size, number, tumor formation with pyloric stenosis, or occlusion, etc.); and (2) we may consider whether the gastric tuberculosis is a solitary manifestation of a tubercular process or a secondary development of a later stage of intestinal infection, such as is frequently found in the advanced stages of pulmonary tuberculosis.

The general hygienic measures, such as preventing the swallowing of sputum and other precautions prescribed in tuberculosis, should also be recommended in the gastric form. In cases not too far advanced, tuberculin treatment, if used with caution, is worth trying. Where motor

insufficiency exists, and it is not contra-indicated by coexisting pulmonary and intestinal affections, operation may be attempted.

CONSTITUTIONAL DISEASES WITH ORGANIC LESION (GASTRIC ULCER)

Although ulcus ventriculi is an anatomical disease, it should not be considered a genuine, primary organic entity. It is an organic disease developing on a constitutional basis, as do the other members of this group with functional disturbances only. It may also be classified with constitutional diseases if a special group is to be segregated, that is, "constitutional diseases with anatomical lesions." Ulcus ventriculi is, however, in a class by itself, for morphologically it sets up an organic disease, though its etiologic and pathogenetic characteristics viewed prognostically and therapeutically range it with the functional diseases.

The significance of the constitutional factor in gastric ulcers has been amply demonstrated and is confirmed by the fact that it usually develops in individuals of habitus asthenicus universalis (Stiller), those presenting vagotonia (Eppinger-Hess), status lymphaticus (Stoerck), or hereditary familial predisposition (H. Strauss); it also appears in association with neuroreflectoric spasms of the gastric musculature (Bergmann, Roessle), with amyxorrhea (Kaufmann), and frequently where there are preëxisting functional disorders of secretion (hyperchlorhydria). Hypersecretion is often a sequel to the manifest ulcer.

Its constitutional characteristics are mainly evidenced by clinical experience which has shown that its successful treatment or even its surgical resection does not mean complete and final healing; the ulcer can be cut out, but the constitutional factor, the predisposition to ulcer formation, still persists. This is the strongest contra-indication to the surgical treatment of gastric ulcer.

Whatever ideas one may harbor in regard to the pathogenesis of gastric ulcer there can be no doubt but that the irritative secretory disorder plays a prominent rôle here. Whether the secretory disorder is the underlying cause or merely accompanies the formation of the ulcer, its presence is responsible for the development and the chronicity of the ulcer and its successful treatment is a *conditio sine qua non* for a permanent cure.[1]

[1] In considering the etiology of acute and chronic peptic ulcer of the stomach and duodenum consideration must be given to the results of the experimental work of Rosenow. Our clinical experience working with Rosenow shows that streptococci gain entrance to the blood-stream from confined infection about the jaws, sinuses of the head and tonsils, and may cause infection of the submucous tissues of the stomach and duodenum. The microörganisms cause thrombosis or embolism of the arteries of the submucosa and consequent hemorrhage into the tissues. The submucous tissues are

The treatment of hyperacidity and hypersecretion means prophylactic treatment of the ulcer. We do well to keep this in mind when the advent of hemorrhage has manifested the presence of the ulcer. Erosions and ulcers, when uncomplicated, have a tendency to heal under appropriate treatment, but new ulcers are liable to develop unless the irritative secretory disorder is attended to.

Gastric Hemorrhage

When occult bleeding, as first described by Kuttner, later by Boas and others, indicates the presence of erosions and ulcerations in cases which are suspected of ulcer on account of hyperacidity, hypersecretion, and other symptoms, it is always a wise proceeding to put such patients to bed, restrict their diet to milk or milk and eggs, and have them undergo in a somewhat milder form that treatment which we shall describe for cases with manifest hemorrhages in the form of more or less profuse hematemesis and melæna. In thus giving erosions and ulcerations a chance to heal during the earlier stages of their development such a timely treatment means true prophylaxis in that it prevents the occurrence of profuse hemorrhages with a further development of the ulcer. Particularly with patients who have already experienced large hemorrhages the demonstration of occult bleeding should always form an immediate indication for a rest cure in bed with strict treatment in order to prevent the occurrence of profuse bleeding. The examination of the feces for occult bleeding, when performed under the necessary precautions, serves as an excellent guide in following up these cases. Its result must be negative for a number of days before we can let up on the treatment, that is, before we can allow the patient to get up, to enlarge his diet list, etc. In cases with occult bleeding the rest cure is usually of shorter duration than in cases with more pronounced hemorrhage. On the whole, however, the treatment should be conducted along the same lines; naturally it has to be more strictly enforced and followed up for longer periods in cases with profuse hemorrhage. It should further be stated that the principles of treatment are essentially the same in cases of so-called acute ulcer as in chronic ulcer.

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thus deprived of nutrition, more or less devitalized and the overlying tissue is readily digested by the gastric juice. Acute ulcer occurs and if the microörganisms remain in the tissues healing is prevented and chronic ulcer results. There seems to be no question that ulcer of the stomach and duodenum may occur in the manner described.

There are other causes which diminish the blood supply in local areas of the submucosa of the stomach and duodenum and the overlying tissues may be digested and ulcer result. Infection as a cause of ulcer of the stomach and duodenum is important because it helps to explain the incidence of ulcer, and it also probably explains the difficulty of the cure of ulcer. Uninfected wounds of the stomach heal readily. It is fair to assume that wounds which do not heal are either infected or the blood supply to the tissues at the base of the ulcer is deficient.—Editor.

Manifest Gastric Hemorrhage [2]

The treatment of fresh hemorrhage should have as its paramount object the cessation of the bleeding and should then direct all its efforts toward preventing a recurrence of the bleeding. This is best accomplished by securing complete mental and bodily rest. The patient should be kept strictly upon his back with an ice-bag on the epigastrium to control the movement of the stomach and facilitate its contraction. With severe hemorrhage it is often necessary to have the patient keep the same position for days in succession. A full dose of morphin and atropin at repeated intervals greatly helps to quiet the patient and at the same time makes it easier for him to stand the fasting of the following days. It is essential to give the stomach absolute rest by abstaining from nourishment. With profuse hemorrhage it is usually better even to omit rectal feeding during the first few days, because nourishing enemata may provoke gastric peristalsis and are said to stimulate gastric secretion (Umber). For the same reason the customary taking of ice pills should be forbidden. We must remember that with any functional activity of the stomach a freshly formed thrombus may easily be dislodged or dissolved. The danger arising from such an accident is certainly greater than the danger from starvation.

In the majority of cases the bleeding comes to a standstill during such a period of complete rest. Unluckily physicians are often inclined to give too much active treatment and disturb rather than assist the natural tendency to thrombus formation. In dealing with gastric hemorrhages we find it necessary to point out the dangers connected with various methods of treatment, which are sometimes greater than the danger from the hemorrhage itself. Often the advent of hemorrhage frightens not only the patient, but the physician as well. The physician, however, should remember that fatal hemorrhage from gastric ulcer is comparatively rare, probably not more than 1 to 3 per cent of the patients dying during hemorrhage. This is shown in statistics of men who personally have followed a large series of ulcer cases (Fenwick, Leube, Ewald, Jacoby). *Bleeding* and *hematemesis* are more common, and the death-rate from them is higher than has previously been supposed (Finsterer). According to Bulstrode's statistics, in 2½ per cent of the chronic ulcer cases death was due to bleeding, forming about 13 per cent of the total fatalities from ulcer. Kelling found 12 per cent and Sherren mentions a 6 to 12 per cent mortality due to hemorrhage in gastric ulcer cases. The physician does well to keep this in mind, particularly when confronted with hemorrhage of a severe type. With moderate hemorrhages the immediate danger to

[2] Part of this chapter is taken from an article by the author: The Treatment of Hemorrhage from Gastric Ulcer.

life is not great, although they may become dangerous when often repeated, thereby gradually undermining the vitality of the patient. The special indication for treating surgically cases with repeated bleeding will be discussed later on. Since we are dealing here with the *direct* treatment of active bleeding we merely want to point out that moderate hemorrhages have a natural tendency to stop. The same tendency is observed in cases with very profuse bleeding. The severe anemia resulting from the sudden great loss of blood brings about changes in the system which, if undisturbed, of themselves tend to arrest the bleeding. The vasoconstriction which goes with the advent of sudden anemia and with syncope allows the bleeding vessel to contract, and the low activity of the heart permits the formation of a thrombus.

The formation of a thrombus is particularly necessary in those cases of chronic ulcer "where the eroded artery lies like a rigid pipe in the fibrous wall of the ulcer, and being unable to contract can only become occluded by the process of clotting" (Fenwick). When the clotting is not quickly and efficiently accomplished such patients may bleed to death very rapidly. A postmortem examination may show that the ulcer, after penerating through the whole gastric wall, had eroded a larger branch of the arteria pancreatica or lienalis, or one of the main arteries itself. The finding of the anatomical conditions demonstrates that probably no medical treatment could have checked the bleeding and, on the other hand, leaves it often very doubtful whether surgery could have accomplished it. Owing to the rapid course in most of these cases we usually find the patient so exsanguinated that the result of an operation becomes very problematical, especially when we consider the great difficulties that are often met with even postmortem in trying to locate the bleeding. We must remember that excessive bleeding not only originates from eroded arteries at the base of the ulcer, but also from ruptured veins around the ulcer, or from minute erosions at distant points, so that even resection of the ulcer may fail to remove the source of bleeding. Without denying the possibility of checking the bleeding by surgical means the conditions present are, as a rule, unfavorable for a successful operation. We must therefore resign ourselves to the fact that a certain number of cases are lost, no matter what treatment we may try. Luckily these cases are not frequent, as we learned from the small total percentage of fatal hemorrhages already stated.

In dealing with excessive hemorrhage we should not be influenced too much by such experiences. We do far better to base our plan of treatment on the knowledge of what actually happens when the bleeding comes to a standstill. As we have argued before, it is either vasoconstriction or the formation of a thrombus which brings about hemostasis, both processes developing with the effect of anemia and the weakened action of the heart. Nothing seems, therefore, more out of place than the routine treat-

ment usually met with, which directs all efforts toward overcoming the depressed condition of the circulation. The attempt to strengthen the weakened heart by administering heart tonics, infusions of salt solution, etc., is greatly overdone by most physicians; in fact, it dominates as a rule the whole plan of treatment. When the desired effect of energetic stimulation has been reached, the vigorous action of the heart will eventually result in freeing of freshly formed thrombus and thus cause a renewal of the bleeding. Since the continuation of the bleeding forms the main danger of such situations, it is obvious that energetic stimulation may increase the danger by bringing about exactly what we should try to prevent. It is therefore unwise to resort indiscriminately to vigorous stimulation. We should be very reluctant with stimulation, employing it only in case of stern necessity, and even then cautiously and judiciously. We are all the more justified in abstaining from energetic stimulation, as general experience teaches that most cases with profuse hemorrhage, when not ending fatally on account of uncontrollable bleeding, overcome anemia and disturbance of circulation surprisingly well.[3] We could quote a number of instances which confirm the experience of other observers that such patients recover from apparently hopeless conditions once the bleeding has come to a standstill. Since the stoppage of the bleeding is the paramount issue of the situation we should avoid disturbing it by undue stimulation.

Physicians of a former generation actually performed venesection when confronted with uncontrollable hemorrhage, expecting to have the bleeding stopped by the resulting syncope and its effect upon the circulation. I saw my teacher, Kussmaul, successfully carry out this principle in a case of extreme hemoptysis. We find the same principle in another method, which, less heroic than venesection, tries to imitate its effect by applying elastic ligatures to the four extremities, thus causing anemia of the internal organs by the accumulation of great quantities of blood in the limbs. This method has been successfully employed in cases of severe gastric hemorrhage. Thus we see that methods which for a time depress the circulation and lower arterial pressure permit the formation of a thrombus and are therefore of greater advantage than heart tonics and vasoconstrictors.

When the thrombus is not formed and hemorrhage continues, the question arises: What can we do to check the bleeding? The general tendency is to give local treatment aimed at stopping the hemorrhage.

Drugs.—Morphin hypodermically is the principal remedy, though opium, pantopon, atropin, belladonna, eumydrin or papaverin can be used in its place either combined or in alternation.

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[3] It may sound paradoxical, yet it is a fact that just those cases of chronic ulcer, which at one time or other have a very profuse hemorrhage, give the best end results both in regard to the palliative and the curative treatment of the ulcer.

As the use of papaverin is of recent date, it should be accorded a separate discussion.

Papaverinum Hydrochloricum.—This may be given in doses of 3 cg. (½ gr.), three times a day, in the form of powder or pills, or by hypodermic injection. Its specific antispasmodic effect has been demonstrated by Pal in experiments upon animals; and later by Holzknecht and Sgalitzer in X-ray work. Opinion regarding its usefulness as an antispasmodic is divided and complete denial of its efficacy is not lacking (E. Schlesinger). We have used it in a large number of clinical cases but obtained no very striking results. We use it extensively, mostly in combination with belladonna, atropin or eumydrin. Papaverin reacts not only on the gastro-intestinal musculature, but also on other smooth muscles, especially those of the arteries, for which reason it may be useful in depressing excessive blood-pressure (Poulsson) or the capillary cramps occurring in chronic interstitial nephritis.

All medicaments given for hyperchlorhydria or uncomplicated ulcer may likewise be used, such as alkalis, bismuth, anesthesin, etc.

Bismuth.—The most reliable of the internal remedies is bismuth, which has been extensively employed in the treatment of gastric ulcer since Kussmaul and Fleiner's recommendation. The crystalline bismuth subnitrate is preferable because, as Matthes has shown, this salt sticks to the surface of the ulcer, accumulates there, and by making a protective coating for the ulcer allows the blood to agglutinate to the bismuth mass. While not sufficiently astringent to cause constriction of the blood-vessels bismuth aids in the coagulation of the blood and at the same time is soothing to the stomach. Thus its effect is opposite to that of the more active astringents. Bismuth should be given in large doses (1 to 2 teaspoonfuls) in every case. It acts best when administered after the stomach has been cleaned out by lavage.

Naunyn reports a case in which lavage of the stomach, followed by the administration of bismuth, stopped a profuse gastric hemorrhage; but the patient, who at the same time suffered from excessive diarrhea, died. Autopsy showed that the ulcer was filled by a clump of bismuth about 20 gm. in weight, almost the total amount taken. This demonstration of the efficient action of bismuth when the stomach is previously emptied by lavage leads us to the discussion of the method which I consider of greatest importance in the control of gastric hemorrhage, namely, gastric lavage.

Barium sulphuricum purissimum (Merck) can, according to the observations of Galambos, be therapeutically employed for the *same purposes and with the same result as can bismuth.* Its protecting and incrusting effect upon ulcers or filling defects has been fully demonstrated by X-ray observation, and the therapeutic usefulness of bismuth lies also in its protective, and not in its astringent or antacid effect (Bastedo). It can

be advantageously used because: (1) it is very low in price (which is very important, especially abroad); (2) it is harmless, due to its total insolubility (as it is one of the least soluble of compounds); (3) it does not darken the stools, as the bismuth salts do, so that it is easy for the patient himself to observe his feces, and also makes possible the recognition of the presence of melena.

While all these medicaments exert only an *indirect* effect on the bleeding a *more direct* influence is exercised by the following drugs:

According to Bastedo in order to accelerate blood-clotting, we may use whole blood; serum, or some of its derivatives; coagulen, a blood-platelet preparation; or cephalin, an extract of brain, marked also as thromboplastin. *Whole blood* is used in the form of transfusion (see Transfusion). *Blood-serum* is not a powerful coagulant even in amounts up to 200 c.c. or more, intravenously administered. It has a certain value, but also the disadvantage of exposing the patient to the danger of anaphylaxis (Bastedo). *Coagulen* (Kocher-Fonio) is useful in a 10 per cent solution and can be given hypodermically, intramuscularly or per os. Its dose is 20 to 60 c.c. of the solution. It should never be administered in the form of an intravenous injection, as there is danger of thrombosis, and the same is true of *cephalin.*

To increase viscosity, *acacia* in a 5 per cent solution (Locke's solution) (Bastedo) or *gelatin* may be given.

Gelatin.—Gelatin may be given either per os or per clysma, but with very doubtful results by either method. It is more efficacious when used as an injection. As the ordinary sterilized gelatin cannot be freed from tetanus spores, it should be used only in Merck's (20 per cent) original sterilized ampules, employing 20 to 100 c.c.

Calcium.—Since the styptic effect of gelatin is attributed by many to the calcium which it contains, *calcium chlorid* has been recommended in its stead, best administered by clysma, 10 to 20 gm. (2½ to 5 dr.) of a 5 to 10 per cent solution every two hours (Boas). Calcium chlorid can do good only after absorption by rendering the blood more coagulable, and in full doses may prove of value in repeated hemorrhages. But its action is slow and it will hardly exert any influence in profuse bleeding.

Sodium Chlorid.—Hypertonic (10 per cent) solutions of NaCl, first used by van der Velden, can be administered in the form of intravenous injections, in a dosage of 5 to 10 c.c. This may stop bleeding in the stomach, as in cases of internal hemorrhage located elsewhere. A hemostatic effect can also be obtained by the ingestion of NaCl in concentrated solution, which will induce reflex contraction of the blood-vessels by irritation of the vagus termination.

Adrenalin and *pituitrin* should be given in cases with very low blood-pressure.

Adrenalin.—Adrenalin has the advantage that the vasoconstriction produced is followed by vasodilatation which may eventually cause a renewal of the hemorrhage. Still it may prove effective when a thrombus becomes sufficiently fixed before the time of secondary vasodilatation.

Ergot.—Neither have we ever seen any benefit from ergot given hypodermically, which, when given in sufficient quantity, acts as a circulatory stimulant and is as such contra-indicated for the reasons given above.

Of the many remedies employed for that purpose the so-called styptics (acetate of lead, perchlorid of iron, oil of turpentine, tannic acid, etc.) are very unreliable hemostatics, while, on the other hand, they are apt to increase the ever-present and annoying nausea and excite vomiting. The same must be said for the internal use of more modern preparations like ergot, gelatin, escalin, and others.

Escalin.—Escalin (aluminum glycerin paste) was introduced and highly praised as a local hemostatic by Klemperer. Others counsel against its use on account of the bad results which they have observed. All these preparations when given per os are just as likely to cause nausea and vomiting as to stop the hemorrhage.

Neutralon or aluminum silicate can be used instead of, or in combination with, bismuth in a dosage of 2, 3, or 5 gm., three times a day.

For the use of alkalis and anesthesin, the reader is referred to the treatment of hyperchlorhydria and uncomplicated gastric ulcer.

When much blood has already been lost, we should resort to: (1) *hypodermoclysis* with normal saline solution (2 to 3 pints); in extreme cases *intravenous infusion* is indicated; (2) *Murphy's drip,* or Murphy's continuous proctoclysis (called also Katzenstein's Tropf-Klystier-method), the continuous slow administration of physiologic salt solution per rectum, drop-by-drop; (3) *autotransfusion,* with bandaging or elevation of the extremities, raising the foot of the bed (Trendelenburg position), thus forcing the remaining blood into the vital parts; (4) *blood transfusion,* transfer and intravenous introduction of blood from another person, either by the direct or indirect method.

Gastric Lavage.—We have, since we first saw lavage performed in cases of bleeding ulcer at Kussmaul's clinic more than twenty-five years ago, employed this treatment in a series of cases of profuse hemorrhage, in almost every case with favorable result. We have no hesitation therefore in recommending gastric lavage in full agreement with Ewald and Minkowsky as the most expedient means in the treatment of severe hemorrhage, provided it is carefully applied. Weil and Rodemann irrigate with hot water—120° to 130° F.

As we are well acquainted with the aversion which most physicians harbor against this procedure, we shall discuss the pros and cons in detail. The most frequent objection raised against lavage is that it may cause perforation. Perforation, however, takes place only after the ulcer has

penetrated the different layers of the stomach and has led to necrosis of the serosa. This is evident when we examine the anatomical features of the opening. As a rule the opening is small and circular, showing the defect produced by necrosis. We have found this condition in a case that we reported in which perforation set in one hour after the stomach was washed in order to prepare the patient for the previously planned gastro-enterostomy. The same condition was found in similar cases. To our knowledge nobody has ever reported that the perforation opening was a lacerated tear through non-necrotic tissue, a finding which would prove that the perforation was a direct result of lavage. This, too, could occur only by forcibly overdistending the stomach with a great quantity of water, a possibility which we may well ignore if ordinary precautions are observed. With lavage carefully performed the danger of causing perforation by overdistention is out of the question. On the contrary, lavage exerts its greatest benefit by doing away with the real cause of overdistention, by removing the large quantities of accumulated blood, acid secretion, food remnants, and gas which are usually present in such cases, often producing an enormous distention of the stomach. We can therefore dismiss the objection that gastric lavage may cause perforation. If it should happen incidentally that lavage is undertaken just before the threatening perforation actually occurs, the cleaning of the stomach will prove very beneficial in preventing the escape of stomach contents through the perforation, thereby greatly improving the prognosis. In our case, cited before, the good result obtained by resecting the perforated ulcer must to a great extent be credited to this fact. It is well known that the prognosis is better when perforation takes place at a time when the stomach is empty.

A further objection to lavage is that it disturbs the complete rest of the stomach, which, as we have seen before, is essential in order to secure firmly the freshly formed thrombus. This is perfectly correct, when the hemorrhage has ceased and we may assume that an efficient thrombus has been established. However, conditions are altogether different when the bleeding continues, because then either no thrombus has developed, or, if formed, it does not completely fill the opening of the vessel. We know from general surgical experience that such a partially occluding thrombus is often the cause of continued bleeding. The removal of such inefficient thrombi is not only not dangerous, but on the contrary it is a necessity in order to give the bleeding vessel a chance to contract or to form a more efficient thrombus. From what we have seen this explanation holds true for gastric hemorrhage, because we have observed in several instances that the bleeding ceased suddenly during the act of lavage. This shows how unjustified is the traditional rule handed down in all textbooks, that lavage is absolutely forbidden in gastric hemorrhage. It should certainly not be condemned in such general fashion, because lavage may prove the best procedure to stop the bleeding.

Finally comes the objection that the introduction of the tube is difficult and exciting for the patient. When lavage is given by a physician experienced in this method he will overcome the difficulties in inserting the tube, particularly when he wins the patient's confidence by his assurance.

As a rule we have been able to insert the tube even with the patient lying on his back without causing excitement or great exertion. It is advisable to insert the tube just far enough to secure siphonage and to limit the quantity of water used each time to about 300 c.c.

As for the advantages of lavage, we have already mentioned the release of partially occluded thrombi. A further very striking advantage is the benefit of lavage when the stomach is distended by large quantities of contents. These stagnating masses are usually very sour and fermenting, and their presence not only causes nausea and pain, but acts very harmfully by constantly irritating the mucous membrane to intense hypersecretion, thereby further increasing the amount of gastric contents. Again, the fermentation always connected with such conditions invariably leads to pronounced and sometimes to enormous gas distention of the stomach, so that when the tube is introduced the contents shoot out at high pressure, even, as we have experienced, with an explosive sound. It seems hardly necessary to explain how detrimental such a distention is in every respect. No doubt it is frequently the direct cause of the continuation of the bleeding. The removal of the fermenting masses not only relieves annoying symptoms of gastric irritation, but eventually brings about a direct cessation of the bleeding by allowing the emptied vessel to contract and this aids in the occlusion of the eroded vessel. The evacuation of the stomach and the contraction which follows it are of the greatest importance for the improvement of circulatory disturbances. We have seen cases of gastric hemorrhage in which the pronounced symptoms of insufficiency of the heart were due in part to anemia, but to a much greater extent to the pressure of the gas-distended stomach against the diaphragm and heart. In these cases circulation was at once improved when the stomach was emptied, while the anemia remained unchanged. We had a very instructive case of this type fourteen years ago. The patient was a woman aged 30 years. After excessive gastric bleeding the pulse rose to 160, became fluttering, and the heart action was so weak and irregular that several physicians connected with the case considered her at the point of death. The stomach was full and so distended that it almost reached the level of the axilla. After the stomach was emptied the pulse rate immediately came down to 116, the heart action became stronger, and the patient recovered.

The understanding of such conditions has been greatly advanced by the recent study of acute gastric dilatation. Acute gastric dilatation is frequently associated with gastric hemorrhage. It is generally admitted that the most rational and the most effective treatment of acute gastric

dilatation is prompt evacuation by lavage. This holds true for cases of acute dilatation in connection with hemorrhage. We hope that this discussion will encourage physicians to resort more frequently to lavage in gastric hemorrhage than heretofore.

Of the cases of severe gastric hemorrhage which we have successfully treated by lavage we wish to report as an illustration one which is particularly interesting. The patient, aged 39 years, had suffered for 16 years from the gastralgic form of chronic ulcer without hemorrhage. In June, 1906, an abscess in the pyloric region was opened, the gall-bladder was found normal, and it is probable that the abscess had formed after a perforation of the ulcer. Soon after the operation severe gastric symptoms recurred with evidence of pyloric stenosis. Since these symptoms persisted in spite of prolonged medical treatment we advised operation. In June, 1907, Dr. Willy Meyer performed a posterior retrocolic gastro-enterostomy by means of sutures. At the pylorus a hard mass was found, producing partial obstruction. Eight hours after the operation hematemesis set in, which in the following twenty-four hours recurred five times, causing such a very great loss of blood that the condition of the patient became alarming. We decided to evacuate and wash the stomach. At first we obtained large quantities of dark bloody material; then the washings became bright red, showing that the bleeding was still active, when suddenly the water returned clear. Before withdrawing the tube a large dose of bismuth subnitrate was poured into the stomach. The bleeding ceased and an uninterrupted convalescence was followed by a perfect cure.

Surgical Treatment.—In the case cited before, gastric lavage stopped an attack of severe bleeding which followed a gastro-enterostomy, an interesting fact, when we consider that surgeons advise this operation to check excessive hemorrhage. Nor is this experience anything unusual. A number of surgeons in this country and abroad have reported the occurrence of severe hemorrhage following gastro-enterostomy. We mention Mayer, Busch (reporting from Körte's clinic), Clairmont (from von Eiselsberg's clinic), and others. Kocher, in discussing his own similar experiences, confirms Clairmont's view, that the possibility of causing a hemorrhage forms one of the main dangers of gastro-enterostomy, because in certain cases this operation not only fails to stop the bleeding, but on the contrary it may be the direct cause of its occurrence. Kocher therefore advises more radical operations like excision of the ulcer, etc., whenever possible.

In contemplating operative measures we should distinguish more clearly between operations performed for the purpose of perfecting a final and complete cure of the ulcer and those operations which are undertaken for the immediate control of hemorrhage. We shall later on discuss the advisability of radical operations in cases in which the ulcer, not yielding to medical treatment, causes frequent hemorrhages, and thereby

greatly undermines the vitality of the patient. In such cases, however, it is decidedly better not to operate at the time of acute bleeding. Here the purpose of the operation is not to check a given hemorrhage, but to prevent the recurrence of bleeding. The radical operation necessary to accomplish this certainly promises better results when performed after the patient has recovered from a hemorrhage. On the other hand, when an operation is undertaken for the very purpose of checking the hemorrhage, it has to be done while the bleeding is active. This surgical indication naturally arises only with very profuse hemorrhages. Unfortunately just in these cases in which we should expect most success from the operation the conditions as a rule are such that the operation forms a greater danger than the hemorrhage itself. We have already pointed out the fact that, with the rapidly developed exhaustion of these patients, a prolonged operation must become a hazardous experiment. If we want to be reasonably certain of accomplishing anything at all we must undertake radical, that is prolonged, operations. The quickly performed gastro-enterostomy does not answer; it is, as we have seen before, entirely unreliable. As Deaver states, gastro-enterostomy in acutely bleeding ulcers is worse than useless. Prolonged operations, however, are decidedly more dangerous, the percentage of mortality after radical operations being considerably higher than after gastro-enterostomy, particularly when the operation is undertaken under the unfavorable conditions resulting from excessive hemorrhage. When we further consider that even a radical operation does not always succeed in checking the bleeding we cannot conceive that this uncertain and risky procedure lessens the danger of the situation. On the contrary, in profuse hemorrhage the patient stands a better chance of recovery if treated in the conservative manner above described. It is not probable that radical operations undertaken at the time of the bleeding will reduce the 3 per cent mortality usually observed in excessive gastric hemorrhage.

Medical Treatment.—We should try, however, to reduce the mortality by improving the methods of medical treatment.

In this connection we wish to plead once more for the frequent employment of gastric lavage as a direct means of checking the bleeding. It is certainly not superfluous to emphasize the advisability of gastric lavage, when we realize that nowadays physicians can be more easily persuaded to perform a laparotomy than to use the stomach tube. At all events lavage should be tried before an operation is decided upon. While it can do no harm, lavage will frequently check the bleeding and postpone an operation, which may prove necessary for other reasons. We have no doubt that the good results derived from lavage will do away with the deeply rooted prejudice against using the tube in bleeding ulcer.

When the bleeding has come to a standstill all efforts should be directed toward preventing a recurrence. This necessitates absolute immobilization

of the patient for several days, eventually prolonged according to the severity of the case. With profuse hemorrhage the patient should not change his position for many days, and he should be forbidden to sit up when he wants to urinate or defecate.

The ice-bag or an ice-coil on the epigastrium should be continued as long as it is well tolerated and comforting. It is usually more effective when applied intermittently. It should never be too heavy, and, if it annoys the patient although light, cold dry compresses may be applied instead.

Nutriment.—The more profuse the hemorrhage the longer should the patient abstain from taking anything by mouth. In cases of very profuse hemorrhage it may be advisable even to abstain from *nutrient enemata* until one feels reassured that no further bleeding is threatening. The feeling of hunger is usually relieved by morphin and becomes blunted within a few days. When thirst becomes very annoying saline enemata may be given, about 5 to 6 ounces every four hours. Later on they may be given alternately with nutrient enemata. In order to avoid irritation of the bowels nutrient enemata should not be given more often than three or four times during the day at intervals of four hours. During the night the patient should not be disturbed.

One hour before the first nutrient enema is given in the morning the bowels should be cleansed by thorough but gentle lavage of the colon with normal saline solution or with a weak alkaline solution (about 1 teaspoonful of bicarbonate of soda to each quart of water). One must avoid the so-called high enema with large quantities of water, which unnecessarily distends the intestine and causes irritation and, better, wash the bowels in the same manner as gastric lavage is given, evacuating the rectum and the higher portions of the large intestine by a number of repeated irrigations, each of which should not be in excess of 1 quart of water at a time. When successfully carried out one cleansing irrigation is sufficient for the day. There is no indication for repeating the cleansing before each nourishing enema, as is so often advised. Each procedure of that kind means a disturbance for the patient and, furthermore, the frequent cleansing interferes with the absorption of the nutrient enemata. In case a nutrient enema causes irritation of the rectum with gas distention and pain, it is usually sufficient to let the rectal contents pass through a tube, which is inserted into the rectum, and to make the interval before the next nutrient enema is given longer. When the contents show pronounced putrefaction it is necessary to cleanse the colon thoroughly by lavage and then omit nutrient enemata for twenty-four hours, eventually altogether. In order to avoid irritation of the rectum it is in the first place necessary to have the nourishing enemata composed of substances which are non-irritating and to eliminate those which become irritating by undergoing fermentation.

Alcohol, particularly when given concentrated in the form of whisky, as is usually done in this country, is liable to irritate and should be avoided. Spiro demonstrated that all drinks containing 7 to 10 per cent of alcohol when given per rectum provoke an abundant flow of gastric secretion. This is another reason for not using alcohol with nourishing enemata. For the same reason proprietary peptone foods, all of which contain alcohol, are not suitable. Otherwise peptones and albumoses are most suitable ingredients; unchanged albumin (for example, native egg-albumen) is not readily absorbed and often undergoes putrefaction and becomes irritating. Peptones and albumoses are quickly absorbed, and these are not irritating provided they are not given in large quantities. As S. Lambert puts it, "all albuminous food—eggs, milk, and meat broths —should be predigested to a degree of complete peptonization by means of pancreatic extracts and bicarbonate of soda. There is a widespread habit in practice of using this peptonizing process only for milk, and of adding to it only the preparations of meat-peptones which are on the market. The freshly prepared peptonized broths and eggs are as easily made as is peptonized milk and leave no uncertainty as to the amount given."

Meat broth, milk, and eggs are used in different combinations with saline solution and with an addition of sugar or amylum. Amylum is recommended by Ewald, Boas, and others, and is said to be less irritating than sugar. But since amylum has to be converted into sugar before it can be absorbed it seems better to give sugar right off, preferably grape sugar, because all sugar has to be changed to grape sugar before it can be used in the economy of the system. The concentration of the grape sugar solution should not exceed 10 per cent (of the total amount of fluid used in the enema); higher concentrations easily irritate the rectum and cause diarrhea.

Ewald recommends the following formula: 2 tablespoonfuls of amylum mixed with 150 c.c. of lukewarm water or milk, to which are added 1 to 2 eggs, 50 to 100 c.c. of a 15 to 20 per cent grape sugar solution and a pinch of salt. Boas' formula is the following: 250 gm. of milk, yolks of 2 eggs, 1 tablespoonful of red wine, 1 tablespoonful of amylum, and a pinch of salt. Leube gives a number of modifications: (*a*) 250 c.c. of milk and 60 gm. of peptone; (*b*) 250 c.c. of milk, 3 eggs, 3 gm. of salt; (*c*) 250 c.c. of milk, 60 gm. of amylum; (*d*) 250 c.c. of milk, 60 gm. of grape sugar.

We usually proceed in the following fashion: First, we give plain saline enemata. We then add 1 tablespoonful of a concentrated grape sugar solution to each enema, gradually increasing the dose to 2 and 3 tablespoonfuls. When the first grape sugar solution is well tolerated we add 1, later 2, eggs, meanwhile changing the medium by using meat broth instead of saline solution, or taking half of each, or substituting pepton-

ized milk for both fluids. The total amount of the enema, at first 5 to 6 ounces, may gradually be increased, but not beyond 8 ounces for each of three enemata in twenty-four hours. Such a maximum enema may contain 6 ounces of milk (or meat broth and saline solution), 2 eggs, and 2 tablespoonfuls of concentrated grape sugar solution. The addition of 5 to 10 drops of tinctura opii greatly lessens the irritation. We abstain from quoting further formulæ given by different authors. We have to try in each case which of the above ingredients is best tolerated and should rearrange the combination according to the individual tolerance.

Von Leube's meat-pancreas enemata are rarely given nowadays. Pancreas preparations, however, are again recommended to facilitate the absorption of cream which some authors (Meyer, Baum, Strauss) add to the nutrient enema. On the whole, fats are poorly absorbed by the rectum.

That the skeptical attitude on the part of many physicians in regard to rectal feeding is unjustified was lately demonstrated again by exact experimental work done by Gompertz in Lafayette Mendel's laboratory in New Haven. Gompertz found that the rectum is capable of absorbing water, sodium chlorid, and dextrose, and that these substances when absorbed are helpful in nourishing the body and supplying fluids and salts to the tissues. Enemata composed of water, sodium chlorid, and dextrose are thus proved to be rational and, although inadequate for continued nutrition over any considerable time, they are useful in preventing the untoward effects of complete starvation while nothing is taken by mouth. When applied by the Murphy-drip method, 1 to 2 quarts of normal saline plus 5 per cent dextrose solution may be absorbed within twenty-four hours.

When nutrient enemata are not tolerated at all and we wish to prolong the starvation period, some nutritive material can be given hypodermically. Lately W. Kausch and others have been adding 50 gm. of grape sugar to a quart of normal saline solution, giving this by hypodermoclysis. It provides a sufficient amount of fluid, which some authors consider the most essential feature of rectal alimentation, preferring to use only saline enemata instead of full nourishing enemata. When nourishing enemata undergo putrefaction and irritate the bowels we have to be satisfied with giving only saline solution (eventually plus grape sugar) either by rectum or hypodermically. When, however, full nourishing enemata are well tolerated and absorbed, as is often the case, they are of great assistance in the management of gastric hemorrhage and with gastric ulcer, not only during the period of exclusive rectal feeding, but also later on when feeding by mouth is taken up. Usually at first only very small quantities of food are given by mouth, and therefore it is advisable to continue rectal alimentation for a number of days, gradually decreasing the number of nutrient enemata as the amount of food taken by mouth is increased.

The period of exclusive rectal feeding differs: in cases of moderate bleeding one, two, or three days may be sufficient; after profuse hemorrhage it is decidedly better to continue rectal feeding for five to eight or ten days, and even longer when nourishing enemata are well tolerated and absorbed. It is true that the amount of food which can be given by rectum and the amount of it which is absorbed are not sufficient to maintain a nutritive equilibrium, but in cases with profuse hemorrhage the danger of starvation is considerably less than the danger of uncontrollable bleeding. We should further consider that during the enforced complete rest a comparatively small amount of nutritive material is required. Naturally one should not have fixed rules in regard to the period of exclusive rectal feeding. We have to be guided by the state of general nutrition and by the condition of the pulse. It is certainly unjustifiable to continue with exclusive rectal feeding when a patient is greatly underfed and keeps on showing signs of weakened heart action. On the other hand, it is just as unjustifiable to generalize on the method of Lenhartz, who abstains altogether from rectal alimentation and gives food by mouth within the first twenty-four hours after the hemorrhage. Reports to the effect that early feeding by mouth according to the Lenhartz method is apt to cause a recurrence of the hemorrhage and so violate the most important indication, that of preventing further bleeding, are becoming more numerous. Bamberger, in summing up, states very correctly that the Lenhartz method of feeding by mouth immediately after the advent of hemorrhage is a risky undertaking. The fact that it was employed in many cases without causing renewed and fatal hemorrhage does not prove anything against the danger connected with early feeding, but merely corroborates the finding of general statistics, that even profuse hemorrhages have often a tendency to come to a standstill. Most physicians who have taken up and reported about the Lenhartz treatment realized its danger and modified it by letting one, two, or three days pass before starting it. We are confronted here with two dangers, that of fatal hemorrhage and that of starvation. The mistake is not any smaller if we overestimate the one instead of the other. As always in such situations we have to judge each case on its own merits and act accordingly instead of strictly following the same method for all cases, which is not any more recommendable for the Lenhartz method than for any other. When, in carefully watching a case, we observe that the starvation period is well tolerated, that nutrient enemata are absorbed without causing discomfort, that the general condition and circulation remain comparatively good, then it is certainly to the advantage of the patient to continue exclusive rectal alimentation for a period stated above as suitable for the individual case.

In breaking entirely with the usual period of starvation and rectal alimentation, Lenhartz and his pupil Wagner put forward a number of reasons which induced them to plead for the advantages of early

feeding by mouth. In the first place, they claim that early feeding is imperative, because only with improved nutrition has the ulcer a chance to heal, and it takes a liberal amount of suitable food to raise the state of nutrition in these anemic patients, who are often greatly exsanguinated. But it is not only the state of nutrition that is said to be of importance. According to Lenhartz, food given immediately after the hemorrhage has the great advantage of binding acid secretion, and thus preventing it from dissolving a freshly formed thrombus and from irritating the ulcer. Lenhartz further maintains that early feeding prevents distention of the stomach and, on the other hand, that the binding of acid secretion brings about a state of rest for the stomach, because it is the presence of acid secretion which frequently causes peristaltic unrest of the organ. Undoubtedly cases occur in which hypersecretion continues in spite of profuse hemorrhage and greatly annoys the patient by causing pain, gas distention, nausea, and vomiting. We have observed such cases and have always found it helpful to combat the acidity by giving atropin, bismuth, alkalis, albumin water, and eventually milk and eggs, in spite of the hemorrhage.

It is just in such cases that gastric lavage by evacuating the stagnating and fermenting acid contents proves the best method of stopping the tendency to hypersecretion, of fighting gas distention and acute dilitation, and of thus giving the stomach a chance to contract and rest. When the stomach is once emptied in these cases and, furthermore, in the numerous other cases where no distention exists, it seems to us a more rational proceeding to keep the stomach in a contracted condition by avoiding all intake of food and fluid by mouth. When this state of contraction remains unchanged for a number of days it not only is the best means of stopping the bleeding, but also materially adds to the healing of the ulcer, provided the ulcer is not too much indurated. It is certainly of the greatest importance for the safety of the thrombus as well as for the healing of the ulcer that for a number of days the ulcer should not be irritated at all by the acid secretion. In cases where, as mentioned above, hypersecretion continues in spite of complete rest, of full use of atropin, of bismuth, and of alkalis it may indeed be of advantage to neutralize the superfluous acid by giving milk and eggs notwithstanding the recent hemorrhage. Such cases, however, form only a certain percentage and it is not advisable to recommend for general use in all cases a method which is at best considered only permissible in a certain type of case. In most cases by far the safest and the most effective method of avoiding gastric secretion is to set the stomach at rest by avoiding all food intake Since secretion is invariably provoked when food enters the stomach it is a questionable proceeding first to provoke gastric secretion and then neutralize its acidity by giving more food. The lively discussion which followed Lenhartz's recommendation has shown that the views upon

which Lenhartz bases his advice are erroneous in many respects. While under certain conditions early feeding may be permissible, as a general rule it is safer to adhere to the old principle of having the patient fast after the hemorrhage. How many days and, further, how carefully to feed afterward should be decided in each individual case. In determining the amount of food which should be given when nourishment by mouth is taken up again we follow the same principles as those on which the treatment of the non-bleeding ulcer is based. Since the treatment is identical for each condition we shall discuss them under the same heading.

After Treatment of Bleeding Ulcer and Treatment of Non-bleeding Ulcer

The main principle in the treatment of the non-bleeding ulcer is the same as that which governs the treatment of the bleeding ulcer, that is, to give the ulcer a chance to heal by procuring a most complete rest for the stomach and its activity. It is therefore customary with most physicians to have patients with non-bleeding ulcers undergo a rest cure in bed for several weeks and to start the treatment with a period of starvation and exclusive rectal feeding, such as described for the treatment of gastric hemorrhage. The intention is to give the stomach, and with it the ulcer, a chance to contract and remain free from the irritation of gastric secretion. This principle of securing the greatest possible rest for the stomach must remain the guiding one when nourishment by mouth is taken up again. In arranging a *diet* we should always keep in mind that we set out to secure healing of the ulcer by giving the stomach as much rest as possible. For this reason, only such *food should be given as makes the smallest demand on gastric secretion, binds the greatest possible amount of secretion, and leaves the stomach in the shortest possible time.* In the section on Diet in Hyperacidity we shall discuss thoroughly different foods and their preparation with regard to the above indications. We refer to this chapter for details both in arranging a diet during the early period of the ulcer treatment and for the continuation of the treatment over longer periods. We shall point out there that the two foods which best answer the indication are milk and eggs. Next to milk and eggs we find suitable for our purpose soups made of leguminous and other flours, gelatin, oil, butter, and a certain amount of sugar. Various combinations can be made of these different foods in getting up a diet for gastric ulcer cases.

A number of formulæ have been given by different authors prescribing for each successive day exactly the kind of food and its quantity. Most of these diet schemes are considered obsolete nowadays (as the diagrams given von Leube, by Penzoldt, etc.), so that we can abstain from

quoting them. For the sake of reference we quote the Lenhartz formula, which has been discussed so extensively of late.

However, we wish to state most emphatically that the Lenhartz formula is as little suitable for every case as were the older formulas (von Leube, Penzoldt, etc.). In fact, we consider it a fundamental mistake to follow any of these formulæ, each one of which has its distinct disadvantages. In adhering strictly to the program of one or another author and in trying to make the case fit the régime, we meet with greater and more difficulties than when we arrange the diet in each instance according to the needs of the individual case. In doing this we should follow certain principles which are safer guides than a prearranged diet list, which rarely fits the individual case from the start.

The foremost principle, as stated several times, is to secure for the stomach a most thorough and prolonged rest; it forms the keynote for all diet rules in gastric ulcer. In following this principle we should select only such food as taxes neither the secretory nor the motor activity of the stomach. However, not less important than the proper selection of food is the determination of the quantity to be given. It is essential to decide for each case the amount of nourishment which is tolerated by the stomach without taxing it and at the same time is sufficient to prevent unnecessarily prolonged malnutrition. Lenhartz claims that in most cases the ulcer does not heal on account of malnutrition, that these patients, who are underfed and highly anemic when the treatment is started, require more nutritive material than is usually offered them if a reparative process and the healing of the ulcer are to be expected. It is to the credit of Lenhartz to have been the first to emphasize and clear up this point. The proclamation of his method caused a revision of the former diet rules and induced most physicians, including von Leube himself, to increase the quantity of food somewhat more quickly than heretofore. On the other hand, the Lenhartz formula prescribes an increase of food which proves decidedly too much for many cases. Starting on the day of the hemorrhage it provides at the end of the first week for 8 eggs, 800 gm. of milk, 40 gm. of sugar, 35 gm. of meat, and 100 gm. of rice, and keeps on increasing the amount of food with each succeeding day. Such quantities of food may make great demands on the activity of the stomach, and the steady secretion and motor activity which go with the disposal of so much food interfere with the principle of giving the stomach a rest and chance to contract. Authors who have tried the Lenhartz method report that it is often poorly tolerated, particularly in cases with hypersecretion. In these cases it is of the greatest importance to reduce the secretory activity as far as possible, which is certainly not accomplished by constantly taxing the secretory organ. The binding of the acid secretion in these cases is just as well accomplished by frequent smaller feedings consisting of milk and eggs. Thus we see that the Lenhartz treatment in

The Lenhartz Diet Scheme (Wagner)

Food	Days after Last Gastric Hemorrhage																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Eggs (beaten up)	2	3	4	5	6	7	8	8	8	8	at 8	the	most	....	...	...	...	...	...	...	...	...	...	...
							4 beaten up 4 boiled																	
Milk (cold and taken with a teaspoon) ...	200 c.c.	300 c.c.	400 c.c.	500 c.c.	600 c.c.	700 c.c.	800 c.c.	900 c.c.	1000 c.c.	1000 c.c.	1000 c.c.	....	.....	.....	...	...	...	...	...	...	...	...	...	...
Sugar	....	....	20gm.	20gm.	30gm.	30gm.	40gm	40gm.	50gm	50gm.	50gm	....	.....	.....	...	...	...	...	...	...	...	...	...	...
Scraped meat ..	....	....	.....	.....	.....	35gm.	twice 35gm.	twice 35gm.	twice 35gm	twice 35gm.	twice 35gm.	....	.....	.....	...	...	...	...	...	...	...	II Form	...	...
Milk and rice ..	....	....	.....	.....	.....	.....	100gm.	200gm.	200gm	200gm.	300gm	....	.....	.....	...	...	...	...	...	...	...	4 egg:	...	...
Zwieback	....	....	.....	.....	.....	.....	.....	20gm.	40gm	40gm.	60gm	....	80gm.	100gm.	...	...	...	...	...	...	...	...	...	...
Raw ham	....	....	.....	.....	.....	.....	.....	.....	.....	50gm.	50gm	....	.....	.....	...	...	...	...	...	...	...	...	...	...
Butter	....	....	.....	.....	.....	.....	.....	.....	.....	20gm.	40gm.	....	.....	.....	...	...	...	...	...	...	...	...	...	...
Calories	280	420	637	777	955	1135	1588	1721	2138	2478	2941	2941	3007	3073	...	...	...	...	...	...	...	...	...	...

emphasizing the necessity of a sufficient quantity of food often violates the other essential principle of securing a rest for the stomach. While we admit the great importance of a sufficient food supply, we prefer to regulate the quantity according to the needs in each individual case. When we observe a pronounced state of low general nutrition and asthenia, with poor response to treatment and little tendency to recovery, we should try in every way to improve the state of nutrition by increasing quickly the amount of such food as is well tolerated, and make use at the same time of rectal and hypodermic alimentation. Even in such cases we should not follow a printed formula, but in adding to the diet we should carefully feel our way, basing the plan for each day on the results of feeding on the previous day. For the majority of cases, however, it seems to us infinitely better for the final result to consider the principle of giving the stomach a rest as of greater importance than the state of nutrition. Even when the patients lose in weight during the first few weeks they finally gain, even on a restricted diet, once they are freed of their annoying symptoms such as pain, sleepless nights, etc. In the majority of cases the irritative secretory disorder is a greater obstacle to the healing process than subnutrition, which is usually well borne and overcome when the rest given to the stomach brings about the healing of the ulcer. We pointed out before that cases with very profuse hemorrhage often obtain a good final result, probably for the reason that in such cases, in spite of the extreme anemia, rectal alimentation is kept up for long periods and nourishment by mouth is given only very carefully and is increased in quantity very slowly.

In another type of case which is characterized by frequently repeated hemorrhages, and which proves intractable to the ordinary method of treatment, such men as Boas, encouraged by the good reports of English physicians (Fenwick, Anderson, Donkin), have enforced exclusive rectal alimentation and total abstinence from nourishment by mouth for periods up to three weeks, and claim that this very heroic treatment has yielded good results by allowing the ulcer to granulate and heal during the long rest given to the stomach. Similar cases are reported by other authors (Bamberger). We had occasion to observe such a case, in which exclusive rectal alimentation was kept up for four weeks with a splendid and lasting result. These are extreme cases, yet they demonstrate that in regulating the diet we should not be influenced too much by the consideration of subnutrition. The majority of ulcer cases tolerate subnutrition well for a period, and when, during this period, the ulcer is given a chance to heal by complete or comparative rest of the stomach, the final result is better and more lasting, due to the securing of a more solid scar. The prolonged enforced inactivity of the secretory organ is further the best means of breaking the tendency to hypersecretion, which is so often the cause of recurring ulcerations. Particularly in those cases, mentioned before, where

repeated hemorrhages occur is the renewed formation of ulcers often due to the fact that the irritative disorders were not sufficiently subdued by previous milder ulcer cures. In some of these cases only a prolonged enforced inactivity of the secretory organ will avail and should always be taken into account even when such patients are submitted to operations. Such and similar considerations make it at once obvious how impractical it is to follow the Lenhartz or any other formula which gives a set prescription for the quality and the quantity of food to be taken for each day, irrespective of the nature of the case.

The rate of increase of suitable food should in the first place be regulated according to the type of the ulcer. In recent cases and in cases of mild type, although observing all the strict rules given below, we may on general principles progress somewhat more quickly than in a chronic case of old standing, where a prolonged rest of the stomach is really the essential feature of the treatment, particularly in the cases mentioned before, which show a tendency to recurring ulcerations and to repeated hemorrhages. We should proceed very slowly after excessive bleeding.

These general rules should be modified according to the manner in which the individual patient reacts to subnutrition, a poor reaction demanding a more rapid addition to the food. A still more important general consideration on which to base the ratio of increase is the individual tolerance of the quantity of food, which varies greatly with different patients. While some tolerate only moderate quantities at any time and regularly experience discomfort with every attempted increase of food which is otherwise suitable, others get along nicely with every increase which the conditions permit us to offer them.

In arranging and rearranging a diet for gastric ulcer cases we must pronounce as the most important rule, which should be observed under all conditions, that whatever food is given, and in whatever quantity, it should be well tolerated and not cause the patient the slightest discomfort or distress. This paramount rule should always be enforced not only during the early period of the ulcer treatment but also later on, and when strictly observed by the patient will serve him well to prevent a relapse during the course of the treatment and afterward.

In order to comply with this rule it is necessary first to give only one kind of food at a time. The usual procedure is to start with milk, which, as stated before, is the most suitable type of food and which should form the staple diet in every case of ulcer. Since the success of the ulcer treatment depends so much on the milk diet, great pains should be taken to select the form of milk which agrees with the patient. If plain milk causes discomfort it should be modified. The usual advice to prepare peptonized milk by the so-called "cold process" invariably proves a failure. We fully agree with S. Lambert, who states that there is no method of furnishing a quickly prepared, palatable, peptonized milk, and we can only en-

dorse every detail of what he says on this topic in his very lucid article on the Treatment of Gastric Ulcer.

"To peptonize milk requires the constant application of moderate heat for two hours for its preparation, and the product has a disagreeably bitter, unappetizing taste. The modification of milk, by the dilution of top milk or cream, can furnish milk of any desired composition. Milk can be so modified that low percentages of casein can be combined with normal or high percentages of sugar and butter fats. And such modified milk, either raw or peptonized, can be made to agree with any stomach, however peculiar the idiosyncrasy of the patient may be. The popular modification of milk by mixing it with limewater or Vichy water gives a clew to a method which has been most successfully used with children. It is not so much the addition of the alkali, though that is a help to modify the curd formation, as it is the mere dilution which is the essential part. Cow's milk has an average constitution of fat 4 per cent, sugar 4 per cent, casein 4 per cent, and its casein has the peculiarity of curdling in large lumps. This last peculiarity is usually considered the cause of the milk's disagreeing, but the abundance of the curd is an equally important factor in causing milk indigestion and gastric irritation.

"Simple dilution of the milk removes the cause of the trouble, and the use of an alkali as a diluent tends to modify the size of the curd, but there is a loss by the same process in nutritive value by a like dilution of both the butter fats and the milk-sugar. It will be found that stomachs which are the seat of ulcer will often bear fats well, and, although cane sugar is at times a source of acid fermentation, it is found that milk-sugar is usually well borne. The problem to secure a milk which will not irritate is therefore the same as that which has been solved for the artificial feeding of infants, namely, to diminish the proteid and still keep the sugar and fat percentages the same as in normal cows' milk."

A definite milk formula should be selected for the individual case and modified as often as necessary. We have often given with advantage first a mixture of half cream and half Vichy water, from which gradually a suitable milk mixture can be formulated.

Milk should always at first be given in small doses at long intervals and the temperature regulated to suit the taste of the patient. We begin with 1 tablespoonful every one or two hours, gradually increasing the dose or shortening the interval, so that the patient gets at the end of the first week about 250 to 300 c.c. of milk in twenty-four hours. This slow increase is indicated in all severe cases and also when gastric feeding is taken up during the period of rectal alimentation, the latter being gradually reduced as the amount of food taken by mouth is increased. On general principles and when conditions permit it is advisable to follow

this slow increase also in milder cases, although under certain circumstances it may be permitted to progress more rapidly, provided the milk is well tolerated. But even under more favorable conditions the increase should not be made quicker than to raise the total amount for twenty-four hours up to 2 quarts at the end of the second week, the single dose at that time not exceeding 250 to 300 c.c., with regular intervals of from two to two and one-half hours. The necessity of giving the stomach a chance to contract after evacuation forbids the administration of large quantities of milk during the first few weeks. Even later on, when the patient is on the fair way to recovery, and partakes of other food, it is usually better not to give more than 2 quarts of milk per day in order to avoid overdistention of the stomach. We wish to state, however, that we have seen a number of patients who tolerated milk well from the beginning and were fond of taking it, and who were able to take larger quantities (up to 3, 3½, and 4 quarts per day) over long periods with great benefit and a good final result. These are special cases in which the milk cure is a success from the beginning and in every way. For a general rule it is better to stick to the 2-quart limit. When a greater amount of nutritive material is desired we can furnish it in different ways: lessening the dilution of the milk, if permissible, or by adding cooked cereal gruels to the milk; by selecting those articles of food which are less voluminous than milk, yet are capable of binding acid, without provoking secretion, such as eggs and gelatin, and further giving pure cream or butter. Finally soups made by boiling fine flours, and particularly leguminous flours (without, however, using meat broth), which are always a good substitute for milk, and very useful during the latter stages of the treatment, may be taken up during the earlier periods. As a general rule we prefer to start adding such foods after a straight milk period of several weeks, but the necessity for doing so may turn up sooner, during the first few weeks, when milk is too badly tolerated and can be taken only in small quantities or not at all, or when the amount prescribed above seems insufficient nourishment for the case.

Lenhartz combines milk and eggs from the beginning, starting with 2 eggs on the first day, and adding 1 egg every day up to 8 eggs at the end of the first week, an amount well tolerated by most patients, but soon becoming repulsive to others. Senator starts with cream, small lumps of frozen butter and gelatin, prescribing:

℞

Gelatin. alb. puriss.—15.0 :200.0	℥ss :℥viss	
Eleosacchar. pulv.	50.0	℥iss

M. et Sig.—1 tablespoonful every half hour.

The addition of sugar is recommended by several authors, particularly Strauss and Lenhartz, and is useful provided it does not cause fermenta-

tion and gastric irritation. Again, others combine from the start milk, eggs, sugar, and butter (Elsner)—an impractical plan, since it does not permit of judging which article agrees with the patient and which causes the discomfort. We would point out once more that at whatever time other foods than milk are administered, whether during the first few weeks or only after a period of straight milk diet, it should always be a strict rule to add only one other kind of food at a time, so that if it causes any distress the new article of diet or a new method of administration may be ascribed as its probable cause. Whether such articles as we just mentioned are taken up from the start or added after a period of straight milk diet they should be continued for weeks in succession if possible. We must abstain from giving strict rules in regard to specified periods for the one or the other type of food just mentioned.

Instead of consulting a tabulated formula it is a far more reliable and more profitable way of proceeding if we consult the records of the previous day and base the continuation and modification of the diet list on our knowledge of what agrees and what disagrees with the individual patient. In case we find that milk and eggs are tolerated in sufficient quantities we may continue this combination, gradually adding the one or the other kind of fluid or semifluid food, always consulting the taste of the patient. If from the beginning milk makes trouble, and has to be restricted in quantity, we are more liberal with eggs, gruels, and the different flours, etc., so that different patients gradually get an individual diet list, while on the whole restricted to those articles of food mentioned above.

The same general rules should prevail when, after a more or less protracted period, restricted in diet to milk, eggs, gruels, flour soups, gelatin, etc., it is deemed time to allow solid food. First of all we should again observe the rule to make invariably only a single change at a time, no matter how simple, because by strictly adhering to this rule we are always in a position to correct quickly any mistake and prevent relapses in the course of the treatment. It has further been urged, and justly so, that with every more radical change, and the change from fluid and semifluid to solid food must be considered radical, the stools should be examined for occult blood, an excellent control in addition to the one furnished by the subjective feeling of the patient.

In selecting solid food, suitable for the first attempt, and in adding others, when increasing the number, we should always keep in mind the indication, given at the beginning of this chapter, that the food must be of such a character and be prepared in such a way that it taxes the stomach as little as possible. For details regarding the articles of solid food, as well as for the articles of the second group (eggs, gelatin, gruels, and leguminous soups), we must refer to the chapter on Diet in Hyperacidity, where we discussed fully the different articles of food and their methods of preparation. However, we would state here once more the two most essen-

tial conditions which have to be fulfilled. First, that whatever kind of food is selected, whether from the animal or the vegetable kingdom (meat, fish, poultry, vegetables, etc.), it should be boiled, in order to deprive it of its extractive substances which we have learned to know as exciting agents of gastric secretion not only in meats, but also in vegetables. Secondly, all such food, after being boiled, should be finely divided and puréed, if possible. In relieving the stomach of the task of dividing up food we spare its activity in every direction, since less secretion is required, and all food which enters the stomach finely divided makes a quicker egress, thereby shortening the period of digestion. Lenhartz's celebrated diet scheme violates this important rule in allowing raw meat from the fifth day on. A. Schmidt and others have pointed out correctly that the digestion of the undissolved fibrous parts of raw meat means a hard task for the stomach, thus defeating our own purpose.

Personally, we are decidedly in favor of postponing the addition of meat in any form or shape as long as possible. When we are ready to add solid food, we prefer to start with vegetable purées, gradually adding thoroughly boiled rice, purée of potatoes, custards and similar egg desserts, putting fish, poultry, and meat courses at the end of the list.

The time when solid food can be given varies greatly. With recent cases of mild character, who undergo a moderately strict treatment, it is customary and sufficient to keep the patient for two or three weeks on a diet consisting of milk, eggs, gruels, etc., and to start with carefully prepared solid food during the third, fourth, or fifth week according to the nature of the case. We wish to make it clear, however, that with very chronic cases, particularly those which have a tendency to relapse, the diet may with advantage be restricted to fluids and semifluids for much longer periods.

In cases with pronounced chronicity a result can only be expected from medical treatment if the principle of sparing the activity of the stomach is adhered to as long as possible. And the most effective means of sparing the activity of the stomach is strict dieting. This applies not only to cases with frequently repeated hemorrhages, but equally as well to those without hemorrhages. Our own experience puts us fully in accord with those authors (Boas, Fleiner, Best, and others), who find the best results of a long-continued strict dietetic treatment, carried out even at the cost of subnutrition, in eminently chronic cases running without hemorrhages. The most stubborn forms of chronic ulcer are those located near the pyloric outlet and causing the clinical picture of continuous hypersecretion. If we expect to make an impression at all in these cases the usual course of treatment, covering a period of three to four weeks and allowing the patient after this time a more liberal diet including solid food, will hardly avail. We shall discuss this special form of chronic ulcer under the heading of Gastrosuccorrhea, and we mention there that as a rule these patients

gain in weight even on a very restricted diet once they are freed of pain and sleepless nights. We wish to add another observation, which we have made frequently, namely, that there is usually no difficulty in persuading the patient to adhere to the restricted form of diet. Once they find out what it means to be entirely free from discomfort and pain they are only too willing to adhere to the strict regimen. In fact, in a number of such cases we met with objections when we proposed a change after the patient had been on a very strict diet for many months, and in some cases for years. The following case will serve as an illustration: The patient, a man at the age of 60, who had suffered for over 25 years from all the symptoms of chronic ulcer, including a number of hemorrhages, claimed when we first saw him that his circumstances did not permit him to undergo any medical or surgical treatment requiring a rest cure in bed, but promised to adhere strictly to the prescribed dietetic treatment. When we saw him again a year later he was still on his diet, consisting of several quarts of milk, cream, eggs, gruels, and leguminous flour soups, on which he had gained 35 pounds, while, at the same time, losing all the pain and discomfort which had marred his life for a quarter of a century. On the occasion of his annual visit, repeated a number of times, we gradually persuaded him to add purées of some vegetables, rice, custards, and chicken or boiled fish once a week. We succeeded, however, not without difficulty, always meeting with the same objection, that he did not desire to give up a diet which was fully sufficient to sustain his strength and which, on the other hand, had cured him of his chronic and very annoying affliction, so that he was able to attend to his business in proper form and meet his obligations.

To those who are persistent in strictly dieting comes the reward of a cure in not a small percentage of chronic ulcer cases. On the other hand, many failures of the so-called medical treatment must be attributed to the short time given to the dietetic treatment, and to the laxity shown by patients and physicians alike in regard to the dietary after the regulation treatment of from four to six weeks is finished. This applies not only to severe and very stubborn forms of the chronic ulcer. No matter how mild a case we are dealing with, a patient who has once shown symptoms of ulcer should be impressed by the possibility that he may develop ulcers in new situations or suffer a relapse in the old unless he makes up his mind to adhere to strict dieting for at least one or two years and possibly longer. The tendency of this disease to recur can be fought successfully only on the condition that the patient is taught to observe a prophylactic diet, avoiding all the errors which we enumerate in the chapter on Hyperacidity as possible causes of irritative gastric disorders: overindulgence in eating and drinking in general, and in particular, in quantity and in quality (coarse and tough food, spiced and highly seasoned, excess of common salt, alcohol, tobacco, etc.). The prophylaxis should further ex-

tend to a revised mode of living, avoiding overfatigue, both physical and nervous, and undue excitement. Sometimes it is necessary for the patient to change his occupation. A very instructive case is that of a young lawyer who, after several years of suffering from hyperacidity symptoms, had his first very excessive hemorrhage while pleading a case in court. A year later, after full recovery, although advised to stop court work, he tried another case and again in court in the midst of the trial suffered a second, almost fatal, hemorrhage. This time the warning lasted for two years, when he took chances again and for the third time experienced a profuse hematemesis during an exciting trial in court. The last convinced him that he had to give up pleading in court.

Drugs and Other Remedies.—During and after the rest cure, which, in mild cases, should last three weeks, and in more severe cases up to six weeks, treatment by resting and dieting can be supported in different ways.

The application of *hot flaxseed poultices* (or electric pads) proves very helpful in all cases which show neither signs nor tendencies of bleeding (occult blood), particularly in all chronic, indurative forms. Von Leube praises the effect of poulticing, which he considers an important part of the ulcer treatment, and only lately urged its application, claiming that the effect of the treatment actually depends on the regularity and persistency with which the hot poultices are applied. They produce active hyperemia of the stomach and provoke a quicker granulation of the otherwise atonic floor of the ulcer. Before applying the poultices the skin should be soaped and rubbed with alcohol and table salt. After that it is protected by a compress covered on the inner side by a thick layer of borax ointment, for which the following formula is recommended:

℞

Spermaceti		
Ceræ albæ	āā	5.0 gr. lxxvii
Petrolati albi		30.0 ℥i
Glyceriti boroglyceriniæ		15.0 ℥ss

The poultices should be applied as hot as tolerated, and should be changed every ten to fifteen minutes. The constant changing can be avoided by using an electric pad.

The treatment by drugs is to a great extent directed against hyperacidity and hypersecretion, so regularly associated with ulcerations of the stomach, and is therefore essentially the same as that recommended for these disorders. Referring to the above chapters in regard to their administration we wish to give here only a few special points.

Alkalis should be used very liberally at all times, because they not only relieve pain by neutralizing acid, but act curatively by reducing gastric secretion (Bickel). Like others, we have made it part of the routine

treatment to give alkalis from the very first day when anything at all is given by mouth, and even during the starvation period whenever the presence of acid fluid in the stomach requires neutralization. Thus in all cases associated with continuous hypersecretion frequent doses of alkalis are a necessity and should be given day and night. Particularly in those cases does the effect of the alkalis support the acid-binding influence of such food as milk and eggs. The systematic use of alkalis should be continued for long periods of time in all cases of ulcer which show symptoms of hyperacidity and hypersecretion. Alkalis are frequently used in the form of natural mineral waters. A small tumbler of warm Carlsbad water taken in the morning is part of von Leube's ulcer treatment. It can be taken for long periods of time by ulcer patients. Its decidedly beneficial effect, attested to by very conservative observers (Ewald, Strauss, etc.), is in the first place attributed to its inhibiting effect on gastric secretion (Jaworski). One should avoid distending the stomach by giving unnecessarily large quantities.

We wish to state, however, that we have seen some excellent results from a regular *Cur* at Carlsbad in patients who had tried in vain by all other methods of ulcer treatment to get rid of their irritative gastric disorder with recurrent ulcerations. We should not like to dispense with the beneficial effect of the Carlsbad water, and often advise our patients to take a tumbler of warm Carlsbad water in the morning in a course of treatment lasting a few weeks and repeated several times during the year, or to continue its use for months in succession.

Atropin, which Riegel and his pupils consider the most powerful inhibitor of gastric secretion, was used successfully by Tabora in a series of severe chronic ulcers with hypersecretion. Tabora gave hypodermically 1 to 3 mg. (1/60 to 1/20 gr.) daily for from four to ten weeks in connection with a strictly observed rest cure and dietetic treatment, as described above. He claims that the systematic atropin treatment better than any other method fulfills the most important indication of every ulcer cure, that is, to set the stomach at rest. It accomplishes this by its inhibitory effect on the vagus nerve, thereby not only reducing gastric secretion, but also relieving the spastic contraction of the gastric musculature, particularly at the pylorus.

We have used atropin very extensively and can only confirm Tabora's statements, at least for cases which show greatly increased irritability of the vagus nerve. These patients usually show a marked tolerance for large doses of atropin, which may be taken for many weeks in succession without creating any ill effects. This, however, is not true for all ulcer cases. In not a few patients we have met pronounced intolerance for atropin, small doses provoking annoying dryness of throat, disturbance of accommodation, and sometimes creating mental excitement and unrest. Hence, we always start with small doses, beginning with 5 drops of a 1:1,000 solution

(0.01 : 10.0), three times a day, and increase the dose 1 drop each following day until we obtain a full physiological effect. We have found the internal administration more suitable for this purpose and just as effective as the hypodermic application.

The *bismuth treatment* has been extensively employed in ulcer cases since Kussmaul and Fleiner proposed its systematic administration. The action of this agent is manifold and its benefit is derived from chemical as well as from physical effect. Fleiner, Schüle, and others have shown that it reduces gastric secretion, while Matthes demonstrated that bismuth provokes a more profuse secretion of mucus than can be provoked by any other agent. The writers have pointed out the great and important rôle which the increased secretion of mucus plays in the healing of the ulcer. Not less important is the physical effect of the bismuth treatment, inasmuch as it, particularly the subnitrate, when given in large doses settles on the uneven surface of the ulcer, thus giving it mechanical protection. It protects it in the first place against the harmful influence of acid secretion, thus not only preventing pain, but at the same time all the reflex symptoms which go with the irritation of the ulcer and lead to the formation of a vicious circle (hypersecretion, peristaltic unrest of the stomach, pylorospasm, vomiting, etc.). Further, acting as an astringent, bismuth facilitates the healing of the ulcer and its antiseptic qualities inhibit the fermentation of carbohydrates. These many qualities do not come into play in every case and bismuth is by no means a panacea, yet the result of the extensive trial given the bismuth treatment leaves no doubt but that its administration benefits and greatly assists in the healing of the ulcer in a large number of cases.

Fleiner considers the bismuth treatment particularly indicated:

1. During any treatment for ulcer, when the change from fluid to semifluid and from semifluid to solid food causes the slightest discomfort or hyperacidity symptoms.

2. In all cases which suffer relapses after going through a regular ulcer treatment. In these cases it should begin as soon as symptoms appear.

3. In all cases of long standing, in which we may presume the existence of induration and a poor tendency to granulation.

When used methodically it should be given for several weeks, at first every day, after a week every other day, then at gradually prolonged intervals.

The bismuth treatment displays its action to its fullest extent when administered as originally advised by Kussmaul-Fleiner, that is, in doses of 10 to 20 gm. (2½ to 5 dr.) suspended in about 200 c.c. (6 oz.) of water and applied through the tube after a thorough cleansing of the stomach by lavage. When lavage is not indicated 1 teaspoonful of bis-

muth suspended in a tumbler of water may be taken by mouth, preferably three-fourths to one hour after internal lavage has been performed by the drinking of warm Carlsbad water. In cases where a starvation period is observed the best time to begin the use of bismuth is coincident with the return of gastric feeding. Lenhartz starts the bismuth on the day of the hemorrhage, giving 1 to 2 gm. (15 to 30 gr.) three times a day instead of the larger dose in the morning. When given on a fasting stomach by mouth the dose is usually not to exceed a teaspoonful. A number of authors recommend an even smaller dose. We prefer the larger doses and, as mentioned before, find the best results when applying it after gastric lavage. We further favor the subnitrate. We cannot convince ourselves that it is more constipating than bismuth carbonate, while, on the other hand, the subnitrate sticks more readily to the uneven surface of the ulcer and forms a better protective coating.

In place of bismuth Klemperer recommended *escalin,* and Pariser a considerably cheaper mixture of prepared chalk and talcum.

Silver nitrate is a drug time-honored in the treatment of gastric ulcer. Its effect is twofold. In the first place, it is expected to act directly on the ulcer in stimulating granulation. Much more important seems to us the second indication, that of combating by its use the irritative gastric disorder invariably associated with gastric ulcer. We could show that gastric irritability in ulcer cases is to a great extent caused by lack of mucus, a frequent finding, which we have mentioned before as a causative factor in the development of the ulcer. We claim that the beneficial effect of the silver nitrate must be attributed to its power of inducing an increased secretion of mucus. Pawlow demonstrated on dogs with gastric fistulæ that mucus is secreted in very large and at times in enormous quantities, when a 10 per cent silver nitrate solution is brought into the small stomach.

Our clinical observations corroborate the result of the experiment and show that the power of silver nitrate to induce and increase the secretion of mucus can be turned to advantage as a therapeutic agent. The most pronounced effect which follows the administration of silver nitrate is that it reduces gastric hyperesthesia.

Our examinations showed that this is accomplished by an increase of mucus, not, as was formerly held, by reducing gastric secretion. We discuss this topic fully under the heading Hyperacidity, to which we refer for details in regard to technic and indications for the silver nitrate treatment. We can only repeat what we emphatically stated under that heading, that the increased secretion of mucus, which follows the application of silver nitrate, especially by lavage, is the most reliable means of reducing gastric hyperesthesia.

However, the increased secretion of mucus means more than merely the reduction of pain and discomfort. The lack of mucus which so often

is observed with irritative gastric disorders is an important factor in the development of the ulcer.

By continuing silver nitrate treatment by lavage over long periods, gradually increasing the intervals from one day to a week, we have obtained good results in chronic ulcer cases which had stubbornly resisted other methods of treatment, including repeated rest cures and well-arranged dietetic treatment.

We published our views on this point in an article on Amyxorrhea Gastrica.

The *oil treatment* was suggested by Cohnheim, who prescribes 100 to 150 c.c. (3 to 5 oz.) of warm oil to be taken in the morning and smaller quantities (1 to 3 tablespoonfuls) before the midday and evening meals. Cohnheim claims that by forming a protective coating to the ulcer the oil not only relieves pain, but also vomiting and the tendency to pylorospasm, that, while thus allowing the patient to eat, it acts itself as a food, and that finally it reduces gastric secretion.

Not all these claims could be corroborated by other investigators, yet the use of oil has yielded good results in the hands of many. The most constant effect is the relief of pain. This is satisfactorily explained when we consider the frequent lack of mucus in gastric ulcer cases to which we have referred several times. Oil taken before meals spreads quickly over the gastric mucosa and provides it with an artificial protective covering when the natural protective layer of mucus is insufficient. We found that this is just as well accomplished by giving smaller doses, 1 tablespoonful about one-half hour before meals. To most patients it is a hard task to swallow the large quantities of oil advised by Cohnheim, and to many it is actually repulsive, so that they refuse to take it.

When it is intended to use larger quantities it is decidedly better to introduce the oil through the tube into the stomach after lavage has been performed. Especially in those cases in which large quantities are said to be particularly indicated previous gastric lavage is in order for other reasons. Cohnheim recommended the oil treatment as particularly effective in cases with pyloric obstruction. He and his pupils, as well as others, report cures accomplished by the oil treatment in cases where operative treatment for the pyloric obstruction seemed unavoidable.

When we discuss the value of oil in hyperacidity we point out that, with gastric stagnation present, oil easily undergoes fermentation, the acid products of which may create severe gastric irritation. Ewald reports such an experience followed by a profuse hemorrhage. It is therefore essential to clean the stomach thoroughly of all stagnating and fermenting masses before putting the oil into the stomach. Aside from providing a protective covering and thus preventing irritative secretion oil provokes regurgitation of duodenal contents, which are alkaline and neutralize acid gastric contents. Finally, it should be mentioned that

Bassler has used X-ray for the treatment of gastric ulcer in a large series of cases, and claims to have observed marked improvement in many chronic cases and complete healing in the acute ulcers. He reports lessening of hypersecretion, cessation of bleeding and subsidence of pain. We have had no experiences with this treatment.

Gastric Lavage.—In describing the bismuth, the silver nitrate, and the oil treatment we found for each of these methods that the best results are obtained when these remedies are administered through the tube. In nearly all textbooks the general rule is handed down that the introduction of the tube is contra-indicated in gastric ulcer. In this general form the rule is unwarranted. We had occasion before to state this when we discussed the great value of lavage in the direct treatment of excessive hemorrhage, where it may prove the best means of stopping the hemorrhage. After the hemorrhage and, furthermore, in cases which show a tendency to hemorrhages the indication of procuring for the stomach a complete rest makes it advisable to omit gastric lavage, provided we accomplish the task of setting the stomach at rest. Otherwise, for instance, when there is present pyloric obstruction with continuous hypersecretion, the removal by lavage of the stagnating acid fluid is the best method of setting the stomach at rest, even in cases with a tendency to hemorrhage. Instead of provoking hemorrhage lavage will be instrumental in preventing bleeding in such cases. After having employed gastric lavage for over twenty-five years in numerous ulcer cases we can state that we have never seen any harm result from its use. In the first place, we have never observed that it directly brought about hemorrhage of any importance. Small hemorrhages from superficial lesions of the mucous membrane, as frequently found in cases of chronic gastritis, are without significance. We have occasionally siphoned from the stomach blood, present before the introduction of the tube. We obtained good results from a thorough cleansing of the stomach, followed by the introduction of a bismuth suspension before tube was removed.

Our experience encourages us to ask for the abolishment of the firmly rooted prejudice against lavage in gastric ulcer. In doing so, we find ourselves fully in accord with Sahli, Wagner, Bamberger, Rutimeyer, and others, who claim that lavage is altogether too little employed in the treatment of gastric ulcer. In excluding methodical lavage we deprive ourselves of one of the best methods of treatment, which, if judiciously employed, will bring about good results in cases which seem intractable to other methods of treatment. The indications for its employment are many. We mentioned its usefulness in directly combating excessive bleeding and as a means for the administration of remedies (bismuth, silver nitrate, and oil). We further discussed at length the great value of lavage when we are dealing with that group of ulcer cases which presents itself as the clinical picture of continuous hypersecretion (Reichmann's disease). The removal of

the stagnating acid masses is not only palliative, but curative in effecting rest for the stomach. We agree with Rutimeyer and Schmidt, who correctly pointed out that continuous hypersecretion is often provoked by the irritating effect of small food remnants sticking to the surface of the ulcer. Lavage removes this source of irritation. Not less important is the methodical employment of lavage in all cases with more pronounced stagnation and pyloric obstruction. By removing the stagnating and fermenting masses lavage eliminates a constant source of irritation of the ulcer and the gastric mucosa; and, furthermore, by cleaning the ulcer, lavage allows us to bring into full play all those methods of treatment which we have enumerated as devised for promoting the healing process. Finally, the cleansing as well as the medical treatment connected with lavage are the most efficient means of treating the chronic gastritis, which is the underlying cause of the whole process. If we thus succeed in curing the gastritis and the ulcerations we often cure the pyloric obstruction, not only in cases where the obstruction is of a spastic nature, but also when the obstruction is partly caused by inflammatory swelling. When the swelling disappears with the healing of the ulcer, the pyloric opening becomes patent.

[In the treatment of chronic ulcer of the stomach, one must first bear in mind the fact that both acute and chronic ulcer may be caused by hematogenous infection. The source of hematogenous infection is frequently found in alveolar abscesses, infected tonsils and sinusitis. The removal of the focal source is indicated as a primary step to prevent continued bacteriemia and renewed infection of the submucosa of the stomach and duodenum. The infectious microörganisms in the tissues of the wall of the stomach and duodenum will probably disappear in time and especially if the general resistance of the patient is improved by proper hygienic measures. We doubt very much if the use of autogenous vaccines would be of benefit.

In the medical management of chronic ulcer of the stomach and duodenum the method elaborated by Sippy is a rational and practical one. Dr. Sippy believes that the corrosive action of the gastric juice is due to the presence of free HCl. Combined HCl has no corrosive action. Consequently he gives the patient a form of management which will as nearly as possible rid the gastric juice of free HCl. This is done with alkaline powders and at the same time a bland diet with frequent feedings is given. The result of the management is ascertained and the medication is increased or decreased by the use of the stomach tube and examination of the aspirated contents of the stomach at definite periods during the day. The patient is preferably treated in a hospital; is kept in a recumbent posture. The patient is first fed with a small quantity of equal parts of good cream and milk, ½ ounce each, given every hour beginning at 7 A. M. and continued until 7 P. M. The amount of milk and cream is

gradually increased day by day until the patient may take 3 ounces of each or 6 ounces altogether every hour, thirteen times per day.

The alkaline treatment consists of two sets of powders; one of 10 gr. each of bicarbonate of soda and of the heavy oxid of magnesia, and the other of 10 gr. each bicarbonate of soda and subcarbonate of bismuth. The soda-magnesia powder is given at 6.30 A. M., half an hour before the first feeding and is repeated every two hours until 8.30 P. M. The soda-bismuth powder is given at 7.30 A. M. and repeated every two hours until 7.30 P. M. The stomach is aspirated with proper technic at 6.30 or at 9.30 A. M., at 4.30 and at 9.30 P. M., and the test is made for free HCl. If it persists an additional quantity of bicarbonate of soda is given with each powder until such a time as the gastric juice shows no free HCl. When there is great irritability of the stomach, a level teaspoonful dose of subcarbonate of bismuth may be given in the fasting stomach of the morning and after the last aspiration at 9.30 P. M. In the event that there is gastrosuccorrhea the stomach may be aspirated at midnight and also early in the morning. When the gastric contents contain no free HCl during the day a well-cooked cereal is given once, then twice, then three times a day at the hourly feedings and with it is taken the 6 ounces of milk and cream. Soft boiled eggs are added in the same way to other hourly feedings until the patient is upon a bland diet of cream, milk, well-cooked cereal and soft eggs, giving him a sufficient amount of nutritious food to keep him well nourished. Later the patient may have purées of vegetables, baked, mashed and creamed potatoes, creamy soups without a meat stock and later stewed fowl, lamb, veal, boiled and baked fish and other easily digested bland foods. Practically all patients learn how to use the stomach tube without discomfort, and when the patient leaves the hospital he continues to pass the stomach tube at least once a day, preferably at 9.30 P. M., and he makes the simple test for the presence of free HCl in the gastric contents. He may add or diminish the amount of the alkalis taken, dependent upon the presence of free HCl in the gastric contents. The heavy oxid of magnesia in one of the powders is laxative in its effect. More or less of these may be taken, dependent upon the condition of the bowels. Dr. Sippy and his associates have treated a great number of patients with chronic ulcer of the stomach with apparently excellent results.—Editor.]

Surgical Treatment

Surgical treatment has been urged as the reliable way of treating gastric ulcer. The topic has always been one of deep interest to us, since we first witnessed twenty-five years ago a series of gastro-enterostomies performed on the advice of Kussmaul. We immediately took up this new method of treatment, which apparently promised such splendid re-

sults. For many years afterward we enthusiastically advocated early operative treatment in a large number of ulcer cases. But following up our own cases and studying the statistics reported in the literature have gradually made us more and more conservative, for we find that surgical treatment not always fulfills the promise of a cure, while, on the other hand, in the majority of cases medical treatment yields excellent results if only properly and persistently carried out.

In discussing the indications for surgical treatment, we wish therefore first to state that gastric ulcer is essentially a disease for medical treatment. No operative procedure, not even the resection of the ulcer itself, removes the pathological condition which caused the formation of the ulcer and which may give rise to the development of new disturbances after the operation. On the other hand, the various methods of medical treatment which we described are aimed at combating the irritative gastric disorders, which are the main obstacle to the healing of the ulcer, if not its very cause. When properly administered these methods of medical treatment bring about the healing of the ulcer in the vast majority of cases and, if followed up sufficiently by prophylaxis in diet and mode of life, prevent further trouble, thus accomplishing a real cure. No one can doubt but that the great majority of ulcer cases are curable by properly applied medical treatment. On the other hand, while surgery gives splendid results in certain cases, yet in others its results are far from satisfactory. In discussing and comparing medical and surgical treatment the question should not be whether to prefer one or the other on general principles. Both have their field, both their justification and their limitations. By choosing judiciously in each individual case we best advise our patients.

Where medical treatment is sufficient, surgical treatment is at least superfluous. Broadly speaking, then, the indication for surgical treatment comes up when medical methods fail, when the ulcer proves intractable to medical treatment, irrespective of what form of ulcer we are dealing with. We consider it a more correct way to give intractability as a general indication for surgical interference than to arrange indications to meet the different types of ulcer and their so-called complications and sequelæ. Take, for example, the complication usually described as invariably requiring operative measures, pyloric obstruction. When taking hold of such a case, it is not at all obvious from the start whether the obstruction is part of the active process (caused by pylorospasm and inflammatory swelling), or whether it is effected by the scar of a healed ulcer, now properly speaking a sequel of the ulcer. When part of the active process it not infrequently yields to a thorough and persistent medical treatment, so that we are not in a position to decide on the necessity of operating before we have given a serious trial of thorough medical treatment, eventually applying successively and rigorously different methods. Like others, we have fre-

quently seen pyloric obstruction disappear entirely under appropriate and persistent medical treatment in cases which at first impressed us as in urgent need of operation. Nor is this experience unusual or new. Any one who gives himself the pleasure of reading Kussmaul's first article on the treatment of pyloric obstruction and gastric dilatation by gastric lavage will find the report of cures accomplished by this new method in cases of such severe type as we rarely have occasion to observe nowadays. When amenable to medical treatment pyloric ulcer with obstruction should be thus treated. The patient is better off when cured with anatomical conditions unchanged.

And so it is with another group of cases, which is often pointed out as especially adapted to and in need of surgical treatment, the group characterized by frequent hemorrhages. These frequent hemorrhages are apt to create a profound anemia and to undermine greatly the patient's vitality, a prognosis which should make the question of timely operation one of earnest consideration. Yet we had occasion to point out that even these stubborn cases finally yield to persistent medical treatment, although it may require such heroic measures as prolonged starvation and long-continued treatment in its strictest form. In these and similar conditions it will be found that success depends on a conscientious application of medical methods, rigorously carried on for a reasonably long period. Personally we both have become more and more convinced that the many failures of medical treatment must be attributed to superficial application of these methods during an insufficient period of time. Many surgeons have learned the necessity for long-continued medical treatment and insist upon it *after* operations. In not a small percentage of cases, particularly in all cases with an active ulcer still present, operative treatment yields satisfactory results only when followed by a strict medical treatment. If the same strictness be observed before an operation is undertaken not infrequently cures are accomplished which make operation unnecessary.

We have no intention of advocating stubborn persistence in medical treatment in cases where we observe no response to the treatment or in cases where we find the patient losing ground. Certain cases do not present themselves for treatment until the ulcer has developed far and created not only local complications but also a low state of nutrition. In such cases it requires large experience and ripe judgment to decide where the greater danger lies, in immediate operation or in trying first to improve the patient's condition by medical treatment. In cases which are less advanced and permit of deliberating we invariably start with medical treatment and decidedly favor its continuation even over long periods, when we observe improvement and succeed in raising the patient's nutrition and strength. The admonition of the surgeon, frequently heard, not to continue the trial of medical treatment beyond a stated number of weeks, cannot be taken literally. Not the time given to a form of treatment is the deciding

point, but the result gained by the treatment. When we get improvement by medical treatment we are justified in continuing it. No harm can come from a treatment which relieves the patient from suffering and improves his general condition even if no final cure is accomplished by the further continuation of the treatment. In such cases the general effect of long-continued medical treatment stands the patient in good stead, when after all an operation becomes necessary, for example, when medical treatment accomplishes the healing of the ulcer and the gastritis, but leaves a pyloric obstruction caused by scar tissue. It is the general consensus of opinion that operations undertaken under such conditions give the best results. Since following these views, we have had reason to be satisfied with the results of operations, suggested and performed after medical treatment has been carried on over long periods of time (in some cases a full year and longer). While, on the other hand, in thus acting the originally contemplated operation has become unnecessary in not a few cases.

We are all the more justified in taking this conservative stand since we have learned that surgical treatment is neither without danger nor always productive of satisfactory results. In the first place, there is still a high average mortality in gastric operations. The simplest method of operating—gastro-enterostomy—shows an average mortality of 10 per cent, although it is true that particularly gifted and skillful surgeons have a smaller percentage of mortality. Secondly, various complications are apt to follow this operation: the formation of adhesions, vicious circle, peptic ulcer, causing the formation of fistulæ and perforation, closure of the anastomosis, etc., conditions which may prove very annoying and disturbing, and eventually necessitate other operations. And finally, even in those cases which recover successfully from the operation, the result is often far from satisfactory. Our own experience corroborates reports in the literature, that many continue suffering after one and even after several operations, and that a certain number of these patients find their only chance of getting well in observing a long-continued rigorous internal treatment.

Without going into the details of statistics, we can sum up this discussion by stating that surgical treatment in gastric ulcer is not a treatment of choice but of necessity and should be taken into consideration only after a conscientious and persistent treatment by one or more medical methods has failed. The time when operation may be considered necessary differs according to the patient's walk in life, and, furthermore, according to the nature of the case. With patients of the working class the necessity for operating turns up at an earlier time than with those who are in a position to carry out for a long period of time the exacting prescription of a strict medical treatment.

Another consideration which we have always found weighing heavily when contemplating surgical measures is chronic suffering. In the so-

called gastralgic form of ulcer, which runs with constantly returning pains, interfering with the patient's capacity for work and marring his enjoyment of life, we often find the patient willing rather to take the chances of an operation, even with a limited prospect of cure, than to submit patiently to a long period of internal treatment. Under such conditions we put the decision up to the patient, after giving a full exposition of the pros and cons both of the medical and surgical treatment.

We meet persistent suffering in different types of ulcer, in pyloric ulcer with gastrosuccorrhea (Reichmann's disease) which forms a high percentage among our own series of ulcer cases treated by operation, further in the so-called callous ulcer of the fundus, and finally in cases causing malformation of the stomach and adhesions. While intense suffering may lead to an earlier decision in favor of operation, yet we should even in these cases adhere to our principle of first thoroughly trying medical methods. In these conditions, as in others, intractability should form the indication for surgical interference, rather than the type of the ulcer itself. In making intractability the main issue, we get a clearer view of the situation and a more precise and sharper indication. *Defining intractability in its broadest meaning as an indication for surgical interference, it applies equally to all forms and types of gastric ulcer and to all its complications and sequelæ.* It applies to those cases in which the tendency to bleeding is not controlled by medical treatment; to the callous ulcer, which remains a constant source of pain in spite of various "cures"; and to those cases where the suffering is due to pylorospasm uninfluenced by energetic medication. It further applies to all conditions of obstruction, pyloric obstruction and hour-glass stomach, both in cases where the obstruction is partly caused by an indurated ulcer which does not yield to medical treatment, and still more in cases where the stenosis is the effect of scar tissue which is beyond the reach of medical treatment. The less the condition is the effect of disturbed function, which may yield to medical treatment, and the more it is caused by permanent anatomical changes, the more is surgical interference indicated. Taking this view we have had excellent results from the operative treatment of cases where the suffering has been caused by the scar of a healed ulcer.

The choice of the kind of operation to be done should be left to the surgeon for decision, according to the merits of the case and the findings at operation. Only one word about the advisability of *resection.* Resection of the ulcer is recommended as the more reliable method in certain conditions and in others is favored because of the claim of surgeons that about 70 per cent of cancers of the stomach originate from ulcers. If this were so, resection of the ulcer would mean prophylaxis of cancer for many cases. However, clinical experience does not corroborate this claim. We fully agree with Lockwood, who states that in the majority of cancer cases no previous history of ulcer is found. Furthermore, our experience in ob-

serving ulcer cases under our care corresponds with his, that the late development of cancer on an old previous ulcer is rare. As long as the high percentage of cancer developing on old ulcers is not sufficiently proved, its consideration should not weigh too heavily when deciding in favor of resection, which as the more radical operation carries a greater immediate danger. When, however, the anatomical conditions encountered at operation suggest the possibility of developing cancer, resection should be performed if possible.

Complications of Gastric Ulcer

Among the most significant complications of gastric ulcer may be mentioned perforation, bleeding, in its later stage cancerous degeneration, pyloric obstruction, and hour-glass stomach, in rare cases gastric tetany.

Perforation.—Perforation may occur at any stage of the ulcer, either in acute form with alarming symptoms, such as open perforation, or when previously adherent to the adjacent organs, a masked form of perforation may develop, or in more chronic form may produce the picture of ulcus perforans. In Bulstrode's statistics, in a death-rate of 18 per cent in chronic callous ulcer, death occurred in 10 per cent from perforation (over 50 per cent), while MacNevin and Herrick reported 30 cases of death due to perforation among 55 fatal cases.

The results of operation depend upon the length of time which has elapsed between perforation and operation. S. Kirk and J. Sherren have each reported more than a dozen patients operated within from twelve to twenty-four hours, all of whom recovered. The prognosis of operation carried out after the first day is very much less favorable.

Hemorrhage.—The significance of the hemorrhage in gastric ulcer is widely discussed in the first part of this chapter.

Ulcerocarcinomata.—This is one of the most disputed topics; clinicians on the one side, surgeons on the other, bringing the most divergent data in favor of their assumptions and theories. While the clinicians assume that cancerous degeneration of ulcer occurs in only a low percentage of cases, surgeons believe a much higher proportion exists, and regard every ulcer as a potential cancer which should be treated accordingly (Thomas R. Brown). G. G. Gruber and E. Kratzeisen found preëxisting ulcer in only 2.3 per cent of their cancer cases, and cancerous development in 1.5 per cent of the peptic ulcers. Wilson and Carty found 71 per cent and Cole 90 per cent of cancers to be of ulcerous origin. Recently Willson and McDowell (Mayo Clinic) have maintained that gastric cancer rarely develops except at the site of a previous ulcerative lesion. This view is not entirely new, as Zenker thought that all gastric cancers are secondary to some form of ulceration (J. Ewing).

Our experiences are those of the clinicians and we have successfully treated a large series of ulcer cases in which only 1 case showed even the suspicion of cancer. This is very important from the therapeutic viewpoint, as we take a conservative position regarding the surgical treatment of ulcer. Nevertheless in cases in which the degeneration of an ulcer into a cancer is verified, or when only a suspicion arises, exploratory laparotomy is strongly indicated.

Pyloric Stenosis and Hour-glass Formation

Gastrectasia, organic motor insufficiency, pyloric stenosis, etc., are not primary diseases to be discussed under a heading for itself. As these organic diseases *mostly* develop after gastric ulcer, they are discussed in this chapter, though it must be emphasized that we are aware of the fact that these conditions may have etiologically different intragastric and extragastric causes, such as primary diseases.

We apply the clinical term "chronic dilatation" to all conditions in which remnants of food and fluid are found in the fasting stomach, that is, at a time when the organ ought to be empty. This stagnation of stomach contents represents a functional disturbance—a motor insufficiency. It may occur in a comparatively small stomach and again in a viscus which is greatly distended and dilated. The small as well as the enlarged stomach, when showing stagnation, may be in normal position or be displaced either upward or downward. In diagnosing dilatation of the stomach we must separately consider three things: the size of the stomach, its position, and its mechanical ability. Neither the size nor the position is the important factor. A stomach may be deeply situated (*gastroptosis*), and it may be very large (*megalogastria*), and yet perform its motor function perfectly well. On the other hand, a stomach may be high and small and its mobility be insufficient. The salient feature is the evidence of motor insufficiency, that is, stagnation.

In treating this condition all efforts are directed toward overcoming stagnation. Stagnation is the cause of fermentation, thus provoking discomfort, pain, and vomiting, and furthermore it prevents food from reaching the intestines, and so leads to subnutrition and emaciation. Any treatment must aim to remove stagnation and all the suffering connected with it and, still more important, it must succeed in making the stomach pass to the intestines an amount of food sufficiently large to raise the state of nutrition and increase the patient's weight.

We have two principal methods of treatment: (1) medical treatment, consisting mainly of gastric lavage combined with dietetic and medicinal treatment of the underlying disease which causes the stagnation; and (2) surgical treatment, which should be employed when medical treatment proves inefficient.

Whether medical treatment will be efficient or not does not depend so much on the degree of motor insufficiency and stagnation encountered when we first meet the patient as on the nature of the primary disease which caused the stagnation.

We wish to recall here that Kussmaul, when he first recommended gastric lavage as a treatment for chronic dilatation, had succeeded in curing by its application stagnation of such high degree as rarely comes to our observation nowadays. At the same time, however, when he introduced his new method of treatment to the medical world his genius had recognized its limitations. He clearly pointed out that lavage will bring relief, but will not effect a cure, when unalterable organic changes of the gastric wall are the cause of stagnation, or when obstruction of the pylorus is the result of contraction by scar tissue or carcinoma. In a prophetic way Kussmaul suggested forty years ago that the surgeon would invade this realm of therapy.

In considering medical and surgical treatment respectively, the one point to be decided is whether the stagnation is caused by conditions which will yield to lavage, or whether there are present unalterable organic changes which are not amenable to lavage treatment. It is therefore essential first of all to clear up the nature of the disease which is causing the stagnation.

Stagnation is observed in various diseases of the stomach. In the foregoing sections we frequently took occasion to point out the treatment indicated in various diseases (gastritis, gastrosuccorrhea, ulcer, carcinoma, etc.) when associated with motor insufficiency and stagnation. In regard to the details of treatment regarding methods of lavage, dietetic, and medicinal measures, we must refer to the respective sections, since the treatment of the underlying primary gastric disease is the paramount object in the treatment of chronic dilatation. In this section we must confine ourselves to a general survey of the principles of treatment of the different forms of stagnation.

We distinguish between two types of stagnation, one caused by muscular inactivity of the fundus, and the other—which is more frequent—due to obstruction at the outlet of the viscus.

Atonic Dilatation.—Muscular inactivity may be functional in character. We shall mention the occurrence of acute dilatation in cases of gastric atony. It is usually a temporary condition which disappears under appropriate treatment. Some authors claim that *gastric atony* never leads to a state of chronic dilatation. Contrary to this view we believe that chronic dilatation does develop from plain gastric atony, but in comparatively few instances. The treatment is, in every respect, that given for cases of gastric atony, that is, a prolonged rest cure, during which we must try to raise the general nutrition by dietetic measures and by bringing into play different mechanical methods of treatment: gastric lavage,

hydrotherapeutics, massage, electrical treatment, etc. When gastric atony has once led to such a serious state of affairs treatment is usually very tedious and only slow progress, if any, may be expected. To gain quicker and better results different operative methods have been proposed; shortening of the ligaments when the dilatation is associated with gastroptosis; gastro-enterostomy; gastroplication (Bircher, Weir); and even resection of the stomach has been performed (Bloodgood). Our personal experience with operative treatment has not been very encouraging. We must not forget that it is not so much the mechanical condition of the stomach as a state of advanced asthenia of the whole system which causes the stagnation. In such cases the great insult of a major operation usually does not help to improve the asthenia. In our own cases it took the patients a very long period of time to recover from the effects of the operation. We must admit, however, that in cases which do not improve at all under medical treatment operative treatment is justified, particularly when we consider that the pronounced motor inactivity of the stomach may be due to degenerative atrophy of its muscular coat.

Stagnation caused by muscular insufficiency is further observed as the result of *destructive and indurative processes in the wall of the stomach* occurring in the course of peptic ulcer, carcinoma, syphilis, etc. The indications for the medical and for the surgical treatment of this type of gastric dilatation are discussed in the foregoing sections. We wish to repeat here, that in *carcinoma* the radical operation of resection should be attempted at an early date; the palliative operation of gastro-enterostomy, however, only when stagnation is pronounced and not sufficiently controlled by lavage.

In *chronic indurative ulcer* of the stomach wall resection, if feasible, is indicated when persistent medical treatment yields poor results.

Special mention should be made of the stagnation found in *chronic gastritis*. In spite of statements made to the contrary we must insist that there is a form of chronic dilatation caused by chronic gastritis, and we could quote histories of cases which would demonstrate that this form is curable by appropriate methods of medical treatment. In more recent and milder forms, in which enlargement of the organ is caused by inflammatory paresis of the muscular coat, excellent results may be obtained by methodical lavage, dietetic and medicinal treatment, as described in the section on Chronic Gastritis. In advanced cases of long standing, stagnation may be associated with a shrinkage of the viscus, caused by indurative changes of the gastric wall (Brinton's "Cirrhosis of the Stomach," a most serious condition, as a rule hardly influenced by medical treatment, and a poor object for surgical interference, except, perhaps, in those rare cases in which the interstitial process provokes hypertrophy of the pyloric end (Lebert). On the whole it is a sad fact that in such conditions neither medical nor surgical methods of treatment are of great avail.

When lavage relieves the patient its employment should be allowed without restriction; dietetics and drugs should be administered along the lines given in the sections on Depressive Disorders of Secretion and Chronic Gastritis.

Pyloric Obstruction.—Much better results are obtained in every way, both by medical and by surgical treatment, when gastric dilatation is the outcome of *pyloric obstruction.* Here again we must differentiate according to the underlying cause.

When *carcinoma* is the cause of pyloric obstruction it leads to early recognition, thus giving a far better prognosis for operative treatment, which should be considered in every case as soon as a diagnosis is made. As a rule, it is advisable to prepare the patient for operation by a period of medical treatment which should, in the first place, provide a better state of nutrition. We often accomplish this by methodical gastric lavage, which removes stagnating and irritating masses and allows greater quantities of well-digested food to reach the intestines. At the same time we supply the system with large amounts of fluid and some nutritive material (sodium chlorid, sugar, etc.), by nourishing enemata, and by hypodermoclyses. When operation is not possible, or stagnation recurs after operation, gastric lavage is the only reliable method of treatment at our command. In the section on Carcinoma we described how this useful method helps to relieve the patient of his suffering and how it sometimes prolongs his life.

With *gastric ulcer* as the cause of pyloric obstruction we have to consider whether the obstruction is caused by pylorospasm, by inflammatory swelling, or by scar tissue. Pylorospasm is especially encountered in that group of gastric ulcer cases which present the clinical picture of continuous hypersecretion (gastrosuccorrhea). We claim that in these cases the presence in the fasting stomach of large quantities of acid secretion means a state of pronounced stagnation and gastric dilatation. In the section on Continuous Hypersecretion, as well as in the section on Gastric Ulcer, we shall deal at length with the question whether this form of pyloric obstruction should be treated medically or surgically. We shall state it as our opinion that in the majority of cases medical treatment brings about the healing of the ulcer and thereby cures the pyloric obstruction, as far as it is caused by spasm of the sphincter muscle and by inflammatory swelling. We have seen large pyloric tumors disappear, which undoubtedly must have been of an inflammatory nature. Therefore an honest attempt should be made to perfect a cure by medical treatment in all cases of pyloric obstruction which are caused by an active ulcer. For how long a period of time we shall continue medical treatment depends on many different points. We proceed to surgical treatment at a comparatively early date (1) when the patient belongs to the laboring class; (2) when intense suffering continues in spite of strict medical treatment, an indication which

appears especially in cases of gastrosuccorrhea; (3) when the state of general nutrition has greatly suffered and the progress of improvement with medical treatment is too slow to promise an early recovery.

On the other hand, we may continue more patiently to pursue medical methods when we observe a steady improvement, even if it be slow. Conditions are altogether different when the cicatricial tissue of a healed ulcer produces such narrowing of the pyloric ring that it interferes with the passage of food into the intestines. Here surgical treatment is imperative. It is the general consensus of opinion that these cases give the best end results when operated on. From this observation we may derive the consolation that in these cases no harm was done by waiting until the actual process of ulceration had subsided.

Hour-glass Stomach.—Similar considerations as in pyloric obstruction should lead us when confronted with a central stenosis, that is, an *hour-glass stomach*. The X-ray and other modern methods of examination have demonstrated that hour-glass stomachs are much commoner than was known heretofore. In a certain percentage of these cases the disfiguration of the stomach is due to inflammatory hyperplasia and to spastic muscular constriction, which disappear when the active ulcer which provokes these disturbances has healed under appropriate medical treatment. In a greater number of cases, however, the constriction is caused by destructive processes that result in the development of scar tissue, which does not change under the influence of medical treatment. When the obstruction interferes with general nutrition surgical interference is indicated. How apt operative measures are to remove the obstruction is a question which must be decided individually for each case. The surgeon will have to choose his method of operating after inspecting the anatomical conditions when the abdominal organs are exposed.

Extragastric Causes.—Finally, we have to consider dilatation provoked by diseases outside of the stomach. We mention here, in the first place, adhesions to the stomach which develop with inflammatory processes in neighboring organs, particularly in the gall-bladder; secondly, compression of the outlet of the stomach (pylorus, upper part of duodenum) by tumors or constricting adhesions. The treatment is essentially that of the underlying disease, which usually requires early operative measures on its own account. When adhesions continue to interfere with the motor activity of the stomach after the original disease has subsided, their removal by operation often yields splendid results in improving and curing the gastric dilatation.

During the last few years the observations of surgeons, in particular of William Mayo, have clearly demonstrated that *chronic appendicitis* or *cholecystitis* is frequently the instigator of pylorospasm and hypersecretion, causing stagnation of acid secretion (continuous hypersecretion, gastrosuccorrhea). In such cases the removal of the appendix and the opera-

tive treatment of the gall-bladder trouble are indicated, and often bring about a cure of the gastric disease. While fully admitting the great progress achieved by these observations we must at the same time point out that the excellent results thus obtained have caused an overestimation of the frequency of this connection, which is responsible for a great many unnecessary and unsuccessful abdominal operations. We refer to the discussion of this topic in the introductory remarks and in the section on Continuous Hypersecretion.

Treatment.—To give a short summary of *medical methods* we state that its principal function consists in gastric lavage, which removes the stagnating fermenting, and irritating masses. As a rule, it is best employed in the morning to prepare the stomach for the day's work. When the patient is greatly disturbed during the night it is preferable to clean out the stomach in the evening. In aggravated cases (gastrosuccorrhea, carcinoma) it may be necessary to apply lavage in the morning and in the evening.

In cases of stenosis pylori Boas employs lavage of the stomach only to obviate an impending gastric stagnation (*Anfangsstagnation*). He cleans the stomach thoroughly by lavage and then gives appropriate diet. If stagnation persists operation becomes necessary but, if it can be averted, Boas has found continuation of the lavage to be superfluous. Instead of lavage—when operation is contra-indicated—he uses also "dry expression" which he strongly recommends; lying on the right side accelerates gastric evacuation (Marcovic-Perussia). In our opinion the aversion of Boas to the use of gastric lavage in these cases is unjustified, as in our experience gastric lavage proves superior to dry expression for many reasons.

Among useful medicaments olive oil should be mentioned; opinion is very much divided as to its usefulness. The experimental basis for its therapeutic employment was provided by Tabora and Dietlen. They found that after using olive oil there was a marked decrease, even total cessation, of peristalsis, and greatly delayed motility, though the pylorus remained open. Right-sided position (lying upon the right side) accelerated the motility in a "passive" way. Precisely the same prompt effect which was shown experimentally cannot always be found in practice. For example, Boas claims that he has not seen any convincing results from its use, and recommends instead of it the use of fluid paraffin, which has given him seemingly good results.

Solutions of alkalis or of sodium chlorid are used, according to the presence of hypersecretion or of hyposecretion; of antiseptics (salicylic acid, resorcin, thymol, etc.), with pronounced forms of fermentation; of bitters (hops, quassia, condurango, etc.), when we intend to stimulate glandular activity. The same kinds of drugs are given by mouth in the respective conditions. Of other drugs we mention strychnin to stimulate

the atonic stomach, and belladonna or atropin when spastic contractions of the pylorus and peristaltic unrest of the hypertrophic fundus prevail.

In regard to *mechanical methods of treatment* we wish to emphasize that abdominal massage, local applications of electricity, gymnastics, and vigorous forms of exercise are strictly forbidden for all cases which present symptoms of active ulcerative or inflammatory processes. We must recommend great restraint in advising the use of these methods. They are of value only when judiciously employed in cases in which the stagnation is principally the result of atony.

The form of *diet* depends on the nature of the underlying disease. The general principle, which applies alike to the different primary diseases, is this, to select that particular form and type of food which least taxes the activity of the stomach and leaves it quickest in the given condition. No such general rules should be given as the following: to give only fluids in cases of stagnation or only dry food. A modified form of dry diet may be of great value in atonic dilatation, while in gastric pyloric ulcer, particularly when associated with hypersecretion, a fluid diet (milk) may be indicated. Here, as in all other conditions, the proper consideration of the underlying disease will assist us in arranging the details of treatment.

Gastric Tetany

Gastric tetany is discussed here because, in the majority of cases, it occurs as a complication of gastric ulcer and may call for prompt operative treatment.

When tetany and gastric disturbance occur together those cases must first be singled out, in which the tetany is the primary affection with an accompaniment of different—mostly excitomotor—disturbances of the stomach.

Tetany usually develops in those stomach diseases involving benign pyloric obstruction. While Rudinger and Jonas hold that the tetany of gastro-dilatation is nothing more than tetany acquired during an extended period of pyloric obstruction, this assumption has not been corroborated by other investigators who have not found that the simultaneous presence of both conditions is merely the result of an occasional coincidence, but have assumed that a causal connection exists between them.

Various theories have been advanced to explain this syndrome. The writer suggested one which, although discussed in several articles, has not been taken up in the literature. We repeat the suggestion because it offers a basis for rational treatment. Kussmaul, who first described gastric tetany, observed that it occurs in greatly emaciated patients with pyloric stenosis after the frequent vomiting of large quantities of fluid has brought about the diminution of the water in the organism, and as a result of this the drying out of the nerves and muscles, which appealed

to him as the probable cause of the convulsions. The removal of great quantities of fluid from the body is actually the only objective finding regularly observed in cases of gastric tetany. That the syndrome occurs only in cases of pyloric obstruction after large quantities of stomach contents have been removed from the body speaks against the theory that decomposition products formed in the stagnating masses are the cause of the convulsions, aside from the fact that no such toxin has ever been demonstrated.

It is, however, not only fluid which is lost by the frequent vomiting. Bouveret and Devic claim that gastric tetany is observed exclusively in those cases of pyloric obstruction which are accompanied by excessive hypersecretion. While this is not absolutely true, yet in the majority of cases gastric tetany is associated with gastrosuccorrhea. The removal by vomiting of excessive amounts of gastric juice deprives the system of a great amount of chlorin by preventing its resorption in the intestines. The impoverishment of chlorids in the system is demonstrated in these cases by the disappearance of chlorids from the urine, and it seems to me that it plays some part in the development of tetany. This theory is corroborated by experiments of Alonzo E. Taylor, who observed "tetanic seizures in dogs, in which the duodenum is cut across and the ends brought into external fistulæ, so that the gastric contents leave the body; the results might be explained by the assumption that there is in the gastric secretion some substance, a constituent necessary to the intermediary metabolism that should return to the circulation by intestinal resorption." That this substance is chlorin seems probable to me, because gastric tetany is met when excessive amounts of acid secretion are removed from the body by vomiting. If this be so the proper treatment of gastrosuccorrhea means prophylaxis of tetany. When tetany appears we should try to overcome the chlorin starvation by the injection of large quantities of normal salt solution subcutaneously or by the rectum. Of greater importance is the prevention of recurring attacks by removing the cause of the trouble. To our conception the underlying cause of the whole trouble is the spastic or organic pyloric obstruction which hinders the passage of the more abundantly secreted hydrochloric acid into the intestine, thus preventing its resorption. This obstacle must be removed, and when we find medical methods ineffective it should be overcome by operation. Tetanic attacks are of serious import and often lead quickly to a fatal issue.

Against the warning of some authors, not to operate in cases with tetany, we would advise that one proceed to operation without losing much time. When Albu claims that therapy offers no remedy which can either check or prevent a recurrence of the tetanic attacks, our theory deserves consideration, since it gives a basis which may prove of great assistance for the treatment of that peculiar and dangerous condition.

Whatever may be the cause of the tetany in gastrodilatation, whether

it is the presence of toxins or the absence of some important chemical constituent (sodium chlorid—Kaufmann), its deleterious properties affect the system through the parathyroid glands and are the cause of their depressory action.

CONSTITUTIONAL DISEASES (WITHOUT ANATOMICAL LESION)

Functional Disturbances

Secretory Disorders.—Before we can arrive at any definite conclusions regarding secretory disorders, we must establish a standard by which we can determine what may be considered as *normal,* so that alterations—either above or below this standard—can be regarded as pathological. How can this standard be established? Shall we say that hyperacidity exists when chemical tests exhibit a high degree of acidity, even when the patient displays no symptoms; or shall we designate as hyperacid the patient who is suffering with the usual complaints, regardless of the degree of acidity found in the stomach contents?

The actual existence of hyperacidity, and the display of symptoms referable to this condition, are by no means identical, and we can only treat those cases which belong to the second class, for the patient without symptoms will give the physician no opportunity to discover the high degree of acidity which may exist in his stomach. In reality we do not treat high-acidity cases—we treat patients suffering from so-called hyperacid complaints—and it may be stated that very often these complaints are erroneously attributed to the coexistent hyperacidity.

Only in a minority of healthy individuals did Galambos find normal secretory values, while a great number who were apparently healthy presented achylia gastrica and hyperacidity. Gerhardt, Nonnenbruch and Rotky, during the World War, found among soldiers in average health that normal acidity existed in but 11 to 28 per cent; while in 9 to 16 per cent anacidity was detected. Subacidity was more frequently encountered than hyperacidity, and this finding agrees with those of other authors who made observations during the War. This may have been due in part to the prevailing state of mental depression and exhaustion. Korach found achylia gastrica in 35 per cent of all stomach cases, but it was claimed that postdysenteric conditions were largely responsible for this high frequency. However, others held a precisely contrary opinion, maintaining that the dysentery was subsequent to a primary achylia, for, the stomach content being deficient in hydrochloric acid, proper bactericidal powers were lacking.

Secretory disturbances of the stomach are of very frequent occurrence

and are encountered in the form of both primary and secondary disorders. In the secondary cases, secretory disturbances of an irritative or depressive character may accompany varied morbid conditions, and are discussed under a special heading.

Primary secretory disturbances in their various forms are manifestations of a constitutional deficiency, frequently indicative of congenital, universal asthenia (Stiller) and can be present, either as a more or less independent disease or, more often, associated with the different symptoms of gastric motor or sensory disorders. They may also manifest symptoms referable to the general condition, to the involvement of other organs, or combined with signs of neurasthenia, hysteria, etc., thus presenting the most variable pictures of seemingly different diseases, which, however, may be correlated by signs which denote their interrelation. Thus achylia gastrica and hyperchlorhydria—which from the chemical or functional standpoint are contradictory conditions—really resemble each other very closely and are only quantitatively different manifestations of a hypersensitive secretory nervous mechanism. In a predisposed individual the two conditions can merge into each other (heterochylia—Hemmeter). But it cannot be denied that besides constitutional factors there are conditional ones also which may influence or provoke alterations in the function of the secretory nerve supply. A multiplicity of etiologic factors can play a rôle and a given set of influences may bring about an outbreak of morbid conditions in a constitutionally deficient individual. The nature of these conditional factors may decide the clinical appearance of the secretory disorders, thus resulting one time in achylia, at another time in hyperacidity. Important among these conditional factors are temperament (excited or depressed), mental condition, the quality and quantity of the foodstuffs ingested, indulgence in alcohol, tobacco and coffee, overwork, worry, etc.

Different climates and races produce individuals more predisposed to disorders of secretory function as a result of disturbance of the equilibrium of their nervous mechanism, who accordingly react more easily with irritative or depressive states. As an example, we may cite the observation that in the United States hyperacidity is more frequently encountered than in middle Europe, while hypo-acidity and anacidity are a comparatively rare finding. In middle Europe decrease and lack of acidity are more common than their opposite.

Treatment.—In the treatment of secretory disorders, it should be borne in mind that as primary diseases they represent functional disturbances, and in their treatment the general rules laid down under the headings of Gastric Neurosis can usually be followed. For symptomatic and local treatment, the special sections on these subjects must be consulted.

IRRITATIVE DISORDERS OF GASTRIC SECRETION

Hyperacidity and Hypersecretion

(*Acid Dyspepsia*)

For various reasons it is preferable to describe in a general way the treatment of the different forms of hyperacidity and hypersecretion. They are provoked by the same causes, the difference in the clinical picture often being due to the individual reaction of different types of patients. In many instances they appear in the same patient at different periods, the more severe disturbance of hypersecretion either gradually developing in a patient who for a long time presented the milder form of hyperacidity, or hypersecretion occurring in acute attacks in people who are habitually subject to hyperacidity. Furthermore, there is a marked difference in tolerating the various degrees of the disorder; in some patients mild hyperacidity creates such severe suffering as we observe in others only when the more advanced types of hypersecretion are present. We even find all the subjective symptoms usually ascribed to hyperacidity in cases with a moderate quantity of secretion of normal acidity. Such pain and discomfort must be attributed to hypersensibility, to lack of mucus, or to both. The indication for treatment depends very much on such factors. We cannot rely entirely on the result of laboratory findings in determining the extent and the duration of treatment, but must always take into account the degree of subjective suffering, the state of nutrition, and the condition of the nervous system.

The general ideas of treatment, however, are the same for all the varieties of irritative disorders of secretion. In order to avoid unnecessary repetition they will be discussed under the heading of hyperacidity, with the understanding that they obtain in the same manner in the other forms of acid dyspepsia. As pointed out in the introduction, the different clinical pictures of irritative disorders of secretion (hyperacidity, alimentary hypersecretion, continuous hypersecretion, etc.) are the outcome of various combinations of the secretory derangement with disturbances of motility and of sensibility. We must always keep in mind that the disturbance of one function easily leads to the derangement of all the functions of the human stomach, and we shall therefore not go too far in differentiating the treatment of the various forms which are usually enumerated to-day. However, after the general discussion we shall take them up singly in order to describe whatever special treatment is indicated in a given form.

The fundamental differences between hyperacidity and hypersecretion should be kept in mind. Hyperacidity or hyperchlorhydria signifies an increased hydrochloric acid concentration as the result of enhanced func-

tion of the HCl secreting glands. Hypersecretion means increased secretory function of the glands in general, not of the HCl secreting glands alone. Accordingly, hypersecretion can be, but is not necessarily, associated with hyperacidity. Hypersecretion may be present in hyperacid, normacid, hypacid, and anacid cases. Hypersecretion is likely to be hyperacid; when it is hypacid or anacid, the possibility of a duodenal regurgitation must be considered. The presence or absence of hypersecretion can usually be recognized by a glance at the ingesta obtained after the withdrawal of a test meal, and even better after the ingesta has been allowed to settle for a couple of hours. Considered separately the acidity figures will likewise indicate the presence of hypersecretion. In cases of hypersecretion the total acidity only slightly exceeds the value of free HCl, while without hypersecretion the quantity of the combined HCl is greater, which accounts for the difference between the two figures.

Hyperacidity.—Hyperacidity (*superacidity, hyperchlorhydria, hyperchloracidity*) is the most common form of dyspepsia. If treatment is to be precise we must first clear up the cause of the disorder. In a great number of patients the derangement is due to an inborn disposition, in others it is the effect of faulty habits, of chronic intoxications, etc., and in a third group it is the result of reflex action caused by disturbances in other organs.

Disposition.—The inborn disposition, the nature of which is still unknown, is not directly amenable to treatment. Such individuals should, however, be taught to avoid certain errors in diet and life which, in them, more readily than in others, provoke the disorders of secretion. Patients of that type are usually of an excitable nature, and since hyperacidity is a disorder of an irritative character everything should be avoided which tends to increase the irritability of the system in general, and of the gastric secretory organ in particular. The necessity of avoiding stimulation of the glandular secretion obtains in the same way in the cases of the second group who, without being predisposed, suffer from hyperacidity on account of faulty habits.

Overwork.—Not a few of the latter group belong to the class of brain-workers who, due to the failure to secure reasonable recreation, either suffer constantly from acid dyspepsia or periodically have attacks after times of unusual and prolonged mental strain and worry. When such people give their systems a chance to rest and to recover they often get rid of their gastric trouble without special treatment. If, however, they continue in their bad habits and keep on hurrying at work and having unreasonable hours of labor without getting a sufficient amount of sleep, we usually see them resort to stimulating their worn-out nervous systems by the use of alcohol, coffee, tobacco, etc.

Abuse of Stimulants.—As far as hyperacidity is concerned this means adding insult to injury, because all the substances named stimulate not

only the whole nervous system, but also gastric secretion by increasing the irritability both of the secretory nerves and of the glandular apparatus itself. Such is the effect of coffee, of alcohol in its different forms, and we think not less pronounced of tobacco.

Hyperaciditas Nicotinica.—The abuse of tobacco may be the only cause of gastric hyperacidity. We have frequently observed that such patients continue suffering until they stop smoking. Experiments in Bickel's Institute (Skaller) showed that tobacco solution hypodermically injected caused gastric hypersecretion in dogs, probably by the direct action of the nicotin on the secretory organ of the stomach. In men hyperaciditas nicotinica is one of the early symptoms of nicotin poisoning and may cause continuous complaints, or come on in paroxysmal crises, sometimes of very violent character. One of my patients who enjoyed perfect health during the rest of the year usually had each spring an attack of hyperaciditas and hypersecretio nicotinica of such a severe type that by suffering and dieting he generally lost as much as 25 pounds in a few weeks, and several times was under the suspicion of developing a malignant growth. Nothing short of complete abstinence from tobacco relieved him.

We believe that the harmful influence of tobacco on gastric secretion is not sufficiently recognized. Lauder Brunton showed that it is more pronounced when tobacco is used on an empty stomach. In cases where moderate smoking is permissible the habit should not be indulged in when the stomach is empty. Not a few of these patients, however, have to make up their minds to stop using tobacco altogether, either temporarily or permanently. Since such pronounced disturbances of gastric secretion may occur in otherwise healthy individuals, it is obvious that tobacco may do a great deal of harm in patients with an irritable system, weakened by overwork and mental strain, especially in the large group of high-strung and excitable neurasthenics, who are constitutionally more susceptible to the toxic effects of tobacco.

The same consideration holds true for the deleterious effects of the other stimulants, *coffee* and *alcohol*. Either of the two is frequently the only cause of the gastric hyperacidity and nothing will avail but the diminution of the harmful stimulant. Not infrequently we have to forbid all these stimulants; sometimes, however, we may allow a moderate use of the one which seems least harmful. We must remember that individuals vary greatly in their toleration of the different stimulants.

Errors in Diet.—Not less important than the abuse of stimulants are errors in diet as etiological factors. Habitual overfeeding plays a great rôle in the development of hyperacidity, especially long-continued excess of protein food, not only in the form of meat, but also of bread. People who habitually take large meals, particularly of food which induces an abundant flow of gastric juice, gradually educate their stomachs to pro-

duce regularly at each meal great quantities of acid secretion. Overindulgence in rich meals leads in the same individuals often to gout or the uric acid diathesis. Here gastric hyperacidity is part of a well-defined disturbance of nutrition, and, without determining whether the gastric disorder is of independent character or only a symptom of the general metabolic derangement, it is essential that a diet should be arranged with a view to improving both conditions. Both conditions require the reduction in quantity of food, particularly of all food articles rich in protein and purin bodies. Some features, however, make it necessary to regulate the diet principally with regard to the condition of the stomach. The diet which we shall later discuss as most suited for hyperacidity will always prove beneficial in combating the metabolic disorders, not, however, vice versa; for example, acid fruits, highly recommended in the treatment of the uric acid diathesis, are often poorly tolerated by patients suffering from gastric hyperacidity and must therefore be eliminated.

Acids.—Overindulgence in acid fruits, acid drinks (lemonade, sour wines, etc.) is one of the causes of hyperacidity. Some stomachs are very sensitive to the effects of acids. They become more sensitive when the irritation causes an increased flow of juice, thereby adding the irritating effect of its own acid secretion. Here in this country indulgence in acid fruits is the more common cause. Very often we observe attacks of hyperacidity develop after fresh fruits have been in season. When eaten ripe and sweet, fruits are generally well tolerated, but most of our fruit is shipped in an unripe, acid condition. The different acids act differently: those present in strawberries, which, when unripe, greatly irritate the gastric mucosa, seem particularly harmful. But there is a wide individual variation in tolerating the different organic acids. Certain people, for example, are more susceptible to the irritating effect of the mallic and gallic acids in apples, while others have discomfort after partaking freely of grapefruit. Experiences of that kind ought to induce people to avoid whatever fruit they have found apt to provoke hyperacidity. The same advice should be given in regard to acid drinks (lemonade, sour wine, etc.) whenever they prove liable to create acid dyspepsia. We have to mention here the now fashionable soured milk and buttermilk. For many people the lactic acid of these beverages is less irritating than any other acid and may be taken with impunity for long periods. Not everybody, however, tolerates lactic acid so well. We have seen numerous patients with a tendency to hyperacidity suffer greatly after an attempt to become accustomed to the use of soured milk. The indiscriminate prescribing of soured milk as a panacea for all digestive disorders often does harm in more than one way.

Condiments and Spices.—Another common cause of hyperacidity is found in the habit of taking too many condiments and spices, common

salt as well as pepper, paprika, mustard, horseradish, sharp sauces, etc., all of which act as exciting agents of secretion.

Iced Drinks.—We should further mention here the irritating effect of ice-cold drinks of every description. Ice water acts as a stimulant to secretion, particularly highly carbonated waters, which, when taken cold, liberate great quantities of CO_2 after reaching the stomach. The stimulating effect of CO_2 makes champagne a provoker of gastric hyperacidity with many people, while others tolerate well the CO_2 in the finer form in which it emanates from champagne. As a rule, however, champagne is just as apt to cause hyperacidity as any other alcoholic drink.

Imperfect Mastication and Coarse Foods.—In many instances the development of hyperacidity can be traced to the imperfect mastication and bolting of food, especially of raw, coarse food, insufficiently cooked, hard vegetables, etc. The effect of insufficiently prepared and poorly masticated food on the stomach is different according to the tendencies in the individual case. To the stomach is given the task of dividing up the food before it is delivered to the intestine for final digestion. Thus in every instance we find it the specific function of gastric secretion to dissolve the framework, thereby effecting a chemical division of the food into its constituent elements. The comminution is effected by the chemical decomposition following the digestive action of the gastric secretion. Thus the gastric secretion in acting upon meat dissolves principally the fibrous tissue surrounding and holding together the muscle fibers and fat, which, after the solution of this fibrous tissue, fall apart. Acting upon bread the gastric secretion dissolves gluten, thus liberating the starch globules (amylorrexis—Strauss). Ad. Schmidt has lately demonstrated that hydrochloric acid acting upon vegetables dissolves the binding substances (pectin, hemicellulose), which form a frame around the individual vegetable cells.

Schmidt's investigations dispose of the prevailing opinion that cellulose and like substances are digested only in the intestines by the action of bacteria. He states that hydrochloric acid in diluted solutions (as found in gastric secretion) dissolves to a certain degree the middle layers between the vegetable cells, which consist of pectin substances, hemicellulose, or young cellulose. When afterwards put in weak alkaline solutions (similar to those in the intestines) the middle layers dissolve completely. The solution does not take place with the reversed order of putting the vegetables first in an alkaline solution and then in an hydrochloric acid solution. This shows the importance of the action of gastric secretion on vegetables, which leads to their chemical division in the stomach into smaller particles and finally into single cells. The digestive effect of gastric secretion on vegetables is of the same order as on meat and on bread; in dissolving and removing the enveloping tissues the constituent

elements are freed and made accessible to the action of the different intestinal and pancreatic secretions.

We shall see later on that, when atony is associated with subacidity, coarse food failing to undergo chemical division may prove heavy ballast, which, by stagnating and fermenting, is apt to increase the motor as well as the secretory enfeeblement of the stomach. With an irritable stomach, however, the presence of coarse food invokes an abundant flow of gastric secretion to effect comminution of the food. This is as pronounced with vegetable as with animal food, and that is probably one of the reasons why so many vegetarians suffer from hyperacidity, although they abstain entirely from eating meat and other animal foods. The great quantities of vegetable food which are usually taken, particularly when ingested raw, necessitate a very copious flow of gastric secretion. Another reason is that certain foods of the vegetable kingdom contain plenty of purin bodies and extractives, which, if not removed by cooking, act as exciting agents of gastric secretion—an interesting illustration of the fallacy of strict vegetarianism, which is recommended as a panacea for all digestive derangements.

Bread.—In connection with vegetarianism, we wish to point out the great frequency of overindulgence in bread as a causative factor of hyperacidity, a point not sufficiently understood by the profession. This is not the place to consider the relationship of starch digestion and gastric secretion. It may be noted in passing, however, that among the victims of hyperacidity are many whose only error in diet is a too liberal allowance of bread, breadstuffs of some kind constituting the principal staple in their diet. Bread should not be classed entirely with the farinaceous foods, because it not only contains starch, but also a great deal of gluten, which represents the frame of the bread and is an albuminous substance. Like the fibrous tissue of meat, the gluten is dissolved by the gastric juice in order to divide up the bread. When great quantities of bread and thus of gluten are ingested they call for an increased gastric secretion in the same manner as do great quantities of meat.

That indulgence in bread proves so harmful in people with a tendency to hyperacidity finds an explanation when we consider that hyperacidity once developed greatly interferes with the digestion of starches by inhibiting too soon the action of saliva. Undigested starch is apt to stagnate in the stomach and act as a constant irritant to the gastric glands. In the most advanced forms of secretory disorder, that is, continuous hypersecretion or gastrosuccorrhea, we often find in the stagnating fluid of the fasting stomach as the only remnant of previously taken food starch globules—clear evidence that starch, although liberated into small granules, stays in the stomach when not sufficiently changed by digestion, and irritates the secretory organ. Such observations support the popular view that what is generally termed bread-dyspepsia is one of the frequent causes

of an acid stomach. The same class of patients are generally fond of desserts, rich pastries, etc. We shall have occasion to discuss how much discomfort the latter create in people with a tendency to hyperacidity.

In dealing with patients afflicted with hyperacidity it should always be our first task to clear up whatever cause is responsible for the disturbance and eliminate it if possible. As mentioned before, the inborn disposition is beyond the reach of our treatment, nor does the struggle of life permit everybody to arrange his affairs in such a way that he can avoid mental strain and worry. But it is within the control of many to abstain from the use of stimulants and from committing errors in diet. This should be particularly enforced when the disturbance comes on periodically, for example, after unusual excitement, at the time of menstruation, etc. In these cases careful dieting during such a spell will greatly alleviate or cut short the suffering. When secretory disorders are of a chronic nature most sufferers from hyperacidity are much better off if they stop altogether the use of the stimulant or the specific food which they have found to act as the exciting agent of secretion in their individual cases. Not a few are so constituted that they have to sail clear of all the stimulants and all the errors in diet which were enumerated before. If these patients wish to be free of discomfort they have to adhere permanently to a diet which others have to follow only when the suffering caused by hyperacidity becomes very annoying. For how long a period the diet should be continued in the latter cases and how strictly has to be decided for each patient individually.

Diet.—Before describing dietetic rules for hyperacidity we wish to make a few remarks which obtain equally in disturbances of other character. In prescribing a diet the physician ought to consider the individual peculiarities of his patients, which vary greatly according to the personal equation. Especially in this country, where we meet people of different races and of various nationalities, brought up under all sorts of conditions, do different habits and modes of living account for many peculiar features of the individual in tolerating certain foods and certain ways of preparing them.

We have never found it a good plan to hand to the patient a printed diet slip which contains the names of a number of articles of food, some of which may be unknown to the patient. We prefer to give general rules in regard to dieting, arranged according to the result of the examination. Then we have the patient give us a list of the different articles of food which he is accustomed to live on and instruct him what he ought to avoid and in what way the articles permitted are best prepared. Proceeding in this way the patient may on the whole continue eating what he is accustomed to, avoiding only the harmful elements. If we have the opportunity of following up a case this method makes it a good deal easier to find out what really agrees with the patient and what disagrees with

him. It takes more time and effort to prescribe a diet in this fashion, but it yields better results. Furthermore we thus avoid recommending food which very often is contrary to the habits of the patient and still more often not to his liking.

In arranging a diet and the treatment of hyperacidity in general we have to consider two indications: (1) *to prevent as far as possible the excess of gastric secretion; and* (2) *to alleviate the suffering caused by the superfluous acid, whenever it appears.* Both indications are equally important and closely interrelated and we shall see that it is best always to consider them both at the same time. When we consult textbooks for general diet rules in hyperacidity we are liable to find directly opposite views in regard to certain foods which are forbidden by the one and allowed by the other. One group of authors recommends a diet consisting chiefly of carbohydrates, while another advises principally food rich in albumins. The such contrary views can be held has its explanation in the fact that the respective authors adhere too strictly to one or the other of the two ideas which are generally followed in laying out a diet for hyperacidity; and, further, that in doing so a faulty interpretation is given of the effect of the two types of food on the gastric function under pathological conditions. The one idea has as its basis the indication for neutralizing the free hydrochloric acid, which is responsible for all the suffering, a task which some physicians think best fulfilled by giving meats, eggs, cheese, and similar food with a great capacity for binding acid secretion. The other idea aims at preventing hyperacidity, and to accomplish this object selects food which demands little secretion. Thus its advocates favor a diet of carbohydrates, because the digestion of carbohydrates is known to require less gastric secretion than that of proteins. On general principles there seems to be no doubt but that the latter indication of preventing increased secretion is the more important and more rational. If we try, however, to arrange a diet accordingly we soon find out that it will not do at all to base the selection of food merely on the results of animal experimentation. While it is an experimentally well-established fact that the digestion of carbohydrates calls for less gastric secretion we must remember that there is a great difference between a dog and a patient suffering from hyperacidity. Hyperacidity is a pathological condition, the irritative character of which manifests itself often in the profuse secretion which follows the ingestion of any and every kind of food. When in such cases starchy foods are taken into a stomach which already contains acid fluid or which quickly answers the ingestion with a profuse secretion the ptyalin action of the saliva is stopped very soon. The ingested starch is liable to stay in the stomach, and since it does not combine with hydrochloric acid, free hydrochloric acid appears at an early period of the digestive act. That, however, is the crucial point of the whole question, because not only does the appear-

ance of free hydrochloric acid provoke discomfort in such cases, but eventually it also interferes with the evacuation of the stomach. Free hydrochloric acid reaching the duodenum causes closing of the pylorus until the acid is neutralized by the alkaline secretions in the duodenum. When the stomach contents consist principally of starches and of gastric secretions this happens very soon and often, because every closing of the pylorus means a delay in the evacuation of the stomach, during which time the amount of gastric secretion is further increased. Eventually when the constant irritation of the duodenum leads to pylorospasm the stagnating acid secretion may create all the annoying symptoms which we are accustomed to connect with hypersecretion and gastrosuccorrhea. This is what we actually observe when we examine the stomach contents of patients with pronounced hyperacidity after they have taken meals consisting chiefly of starchy foods; we find a great deal of poorly digested starch and a highly acid fluid. In the well-known cases of gastrosuccorrhea the stagnating acid fluid of the fasting stomach frequently contained starch globules, often as the only remnant of previously taken food. The correctness of this statement can be verified by any one who will examine such fluids microscopically. Thus we see that the kind of food which theoretically seems the most appropriate not only does not prevent increase of secretion, but actually provokes it, thereby creating all the symptoms which we set out to avoid.

Protein food, on the other hand, by binding acid secretion postpones the appearance of free hydrochloric acid. This means more than merely postponing the subjective suffering brought on by the free acid. The acid which combines with the protein effects its digestion, so far as gastric digestion is concerned, and thereby facilitates its egress from the stomach during the period preceding the appearance of free hydrochloric acid. The smaller the remaining part when free acid turns up, the shorter will be the duration of the secretory activity, which the digestion of the remaining part still requires. This shows that the selection of food which has a great capacity of binding acids may at the same time satisfy the second indication of preventing superfluous secretion. In illustrating the effect of these two types of food we again meet with the problem pointed out on several occasions, that is, that it is faulty to consider merely one part of the gastric function. The knowledge of the action of a certain food on secretion (in animals and healthy individuals) is without value if we fail to recognize the effect it has on the evacuation of the stomach, particularly under pathological conditions. A good deal more is to be said against the tendency to restrict the diet too much to one kind of food, be it carbohydrates or protein. Aside from the experience that most patients cannot be persuaded to adhere for a long period to a one-sided diet, consideration of the state of nutrition generally forbids it. If we except special periods, during which we shall see that a greatly restricted diet is

in place, we find that sufferers from hyperacidity are as a rule better off with a mixed diet, provided the constituents of the diet are properly selected and properly prepared.

In contemplating a mixed diet we have to consider more than merely whether a certain food belongs to the carbohydrate or protein class. As a matter of fact not a few of the ordinary articles of food contain both carbohydrates and proteins as already pointed out for bread. But it is of importance to know how large is the percentage of starches in a given food, how large in a meal composed of different foods, and how large the total amount taken with all the meals of a day. Guided by the considerations given above we prefer to have a preponderance of albuminous food. Yet we shall see that a certain percentage of starches, given at the right time and in the right order, is often tolerated in hyperacidity. While it is perfectly true, on the other hand, that with an individual meal meat causes little discomfort in cases of hyperacidity, it is not advisable to keep patients on a strict meat diet. When meat forms the bulk of the meals it necessarily requires a great total amount of secretion, and when such a diet is kept up for long periods the constant taxing of the secretory organ is bound to lead to hypersecretion. Much depends, therefore, on the proper combination of different food types. For most foods much depends on the method of preparation. By certain preparations food can be changed chemically and physically to such an extent that while inducing less secretion it nevertheless exhibits an undiminished capacity for combining with acids. When meat is boiled instead of broiled it loses the extractives, which act as exciting agents for secretion, but retains the same capacity for binding gastric juice. Again, when it is given minced it taxes the activity of the stomach considerably less than when swallowed in bigger morsels, because it requires less secretion for division and, being already finely divided, it leaves the stomach quicker. In discussing the individual articles of food we shall have occasion to show that these and similar considerations are the most essential in arranging a diet list. For reasons mentioned before we shall abstain from giving complete diet lists. We prefer to discuss individually the principal articles of food, considering how much they provoke gastric secretion, how much capacity they have for binding secretion, in what way they can be prepared without destroying their acid-binding capacity so that they leave the stomach quickly. An ideal diet for hyperacidity should be composed of such food, prepared in such a way that it calls for the smallest possible amount of secretion, that at the same time it is apt to bind all the acid secreted, and that it further leaves the stomach in the shortest possible time, thereby reducing the period of secretion. Often it is a difficult task to prescribe such a diet, yet it should be the goal.

Milk.—The food which best answers these requirements is milk. The principal advantage of milk is its freedom from extractives, which accounts

partly for the fact demonstrated by Pawlow, that of the different forms of proteid food milk induces the smallest amount of secretion, and at the same time fixes the greatest quantity of free hydrochloric acid, and when given in small or moderate quantities at a time quickly leaves the stomach. For all these reasons milk is the most suitable food during acute attacks of the secretory disorder, especially when they are of severe character. In such cases it should constitute the staple diet and should be administered in such a form as will prove agreeable and beneficial to the patient. Patients suffering from hyperacidity often claim that they tolerate milk poorly. Not infrequently the discomfort is caused by errors in administering the milk. It is true that some patients are regularly upset by milk, no matter in what form it is given. Yet most derive the greatest comfort from a milk diet when it is given in the proper way. It is always preferable to give it by itself, without combining it with other food, particularly without bread, which is often erroneously added. When it is the only food it should be given in quantities of 6 to 8 to 10 ounces every two or three hours. We have to find out whether it is best tolerated when taken raw or boiled, as whole milk with the cream or as skimmed milk. Some patients stand it better when it is diluted with one-third to one-half vichy water, while others have to add limewater or other alkalis (sodium or magnesium preparations) to prevent its rapid coagulation in the stomach. This is particularly so when the stomach contains stagnating acid. In such cases it may be necessary first to remove the acid fluid by lavage, the drinking of alkaline waters, etc., before the milk is ingested. If plain milk disagrees, peptonized or malted milk may be tried; sometimes fermented milk (koumiss, matzoon, etc.) is taken well, although these preparations are just as liable to increase the discomfort when containing much acid or much gas, both of which excite secretion. This is still more frequently so with buttermilk and soured milk on account of their pronounced acid condition, wherefore it is safer to exclude them from the diet list. Of other milk preparations we name as usually well-tolerated cream, junket, pot cheese, and cream cheese if taken in moderate quantities.

We have frequently given with very good results cream diluted with a third to a half vichy water, instead of milk, when the latter caused discomfort. This is somewhat in contradiction to the usual recommendation, which lays stress on the high percentage of fat which pure cream contains.

Fat.—We may deal right here with the action of fat, which merits separate discussion. Animal and vegetable fat in the form of cream, butter, oil, and meat fats are highly recommended in hyperacidity, because animal experimentation has demonstrated that fats by reflex action from the duodenum reduce gastric secretion. As with starchy foods, however, the result of animal experimentation cannot be used without properly con-

sidering pathological conditions. When a tendency exists to delayed evacuation of the stomach, fat given in large quantities with a full meal is liable to stagnate with the rest of the food, usually collecting on the surface of the chyme. The stagnating fat eventually undergoes butyric fermentation and the resulting fatty acids act as a very annoying irritant, causing pain and further secretion. This is particularly so with cooked fats, butter sauce, etc., which contain fatty acids before reaching the stomach. We have further to consider the regurgitation of the duodenal contents which, according to Boldireff's investigations, often follows the ingestion of oil and fats into the stomach. While the alkaline intestinal contents may to a certain degree neutralize the acid stomach contents, the action of the pancreatic juice on the fat leads to the formation of fatty acids, which, when produced in large quantities, may give rise to severe disturbances. In not a small percentage of hyperacidity cases fat thus distinctly increases the suffering and aggravates the whole condition, which shows that the indiscriminate recommendation of large quantities of different fats for all cases of hyperacidity is unwarranted. Still, under certain conditions, fat proves very helpful. Much depends, however, on the kind of fat and on the way it is given. Tangl, Erdélyi and Fejer found that fats are evacuated from the stomach in accordance with their melting-point; the higher the melting-point, the slower is their evacuation. In accordance with this fact, olive oil, butter and the fat of geese or ducks are more advantageously given than lard, margarin or lamb fat. When given (best in the form of oil) before meals it readily spreads over the mucous membrane and by sticking to it prevents the intimate contact of the irritant acid secretion with the mucous membrane. This is particularly valuable in gastric hyperesthesia and in cases in which the lack of mucus allows a very close contact of gastric secretion and mucous membrane, a pathological condition described by the writer as amyxorrhea (or better, amyxia gastrica). In these cases in which the lack of mucus often causes hyperacidity symptoms even with a normal amount of acidity, the oil furnishes an artificial covering to the mucous membrane and thereby acts beneficially. Aside from the oil given in this fashion, cream and fresh butter may be taken freely, and in cases without motor complications perhaps tend somewhat to lessen the secretion of gastric juice. One must, however, avoid giving too much fat, as large quantities of oil, butter, or cream soon become repulsive to most people. Butter and cream can easily be taken with other kinds of food. But it is always better to give butter uncooked, even when it is added to fish, vegetables, eggs, etc., instead of boiling it. Cream may also be advantageously given between meals in place of milk, either pure or mixed with vichy water. Other animal fats should be avoided, for example, fried bacon, which, especially when salty, is apt to give rise to acidity. All fried foods are prohibited. It is sometimes claimed that mutton fat

agrees with hyperacidity patients. This is correct for a small percentage of patients, and it should be tried carefully at first. As a rule it is better to remove the fat. .

Eggs.—The fat of the egg yolk is well borne, as is the whole egg. Next to milk, eggs should form the staple element of diet and should be added after a period of straight milk dieting. The white of the egg is an albuminous substance which binds a good deal of acid without provoking much secretion. In cases of great gastric irritability egg-albumen is often retained where even milk is not tolerated. It may be given in the form of albumin water or the white part of a boiled egg may be taken separately. Whether soft boiled or hard boiled depends on the individual tolerance. In some cases it goes best when the egg is boiled for a long period, so that it is hard enough to be ground into a fine powder. Aside from these conditions of great irritability, eggs may be taken in different forms, raw, boiled, poached, with meals and between meals. Hyperacidity patients having a mixed diet often require some food between the principal meals when annoyed at such times by the acid chyme. The acid-binding capacity of eggs makes them an appropriate food, which may be taken with or instead of milk. Eggs can further be used for preparing desserts (custards, soufflés, etc.).

Of other foods rich in protein we have to consider those of the animal and of the vegetable kingdom.

Meats.—In selecting meat, fish, poultry, preference should be given to lean kinds over the fat and oily forms. Pork, certain kinds of fowl (duck, goose, etc.), oily forms of fish (salmon, mackerel, bluefish, eel, pompano, shad, etc.), are usually classed as heavy food, because the thorough infiltration of the meat with fat prevents the access of gastric secretion, causing delay of the digestion of the meat and thereby of its egress from the stomach. The richer in fat the longer the sojourn of the food in the stomach, which prolongs the period of secretion. As belonging with the fat types, we mention beef tongue, tripe, and brains.

Of the lean ones beef is the least favorable on account of its great amount of extractives. The extractives are an excellent stimulant for gastric secretion, which is the reason that meat broth is given with advantage when gastric secretion is sluggish. In hyperacidity, however, meat broth, meat extracts, beef tea, bouillon, etc., should be forbidden. For the same reason the coating of a roast, which is usually very rich in extractives and salts, should be avoided. On the other hand, all meat, fish, and poultry which are boiled lose their extractives while still retaining the same amount of albumin and its acid-binding capacity. We can still further reduce the amount of secretion necessary to digest a certain amount of fish or meat if, after boiling it, we have it minced and puréed so that by hastening its passage through the stomach we shorten the period of secretion. In cases where meat or fish is tried after a period

of diet restricted to milk and eggs, it should at first always be given boiled, finely minced, and then rubbed through a sieve. Patients who are less restricted should always select the lean types, preferably boiled, deprived of skins and other coarse parts which require more digestive activity of the stomach than the tender meat parts.

Of lean meats we name beef (best taken in moderate quantities and not too often), lamb (young), mutton, chicken, turkey, capon (the white meat preferable to the dark meat), squab, partridge, and guinea hen. Veal is allowed only when milk-fed and tender. In this country it is usually too coarse and tough and is better omitted. The lean fish are: cod, halibut, haddock, striped bass, brook trout, red snapper, perch, smelt, whiting, etc. In connection with this class of food we should mention as allowed the soft part of oysters, caviar (if mild and not too salty). Lobster and crabs, although binding a great deal of acid, have too coarse a fiber and thus require too much secretion. Other forms allowed are sweetbreads and tender calf's liver. Kidneys are too hard and tough. Very recommendable is gelatin, the "albumin sparer," which, if not made too rich from added ingredients, calls for little secretion while fixing a good deal of hydrochloric acid. It can be used for making desserts, jellies, which may be flavored with some fruit juice if necessary.

Vegetables.—In selecting and preparing vegetables we are guided by the principles brought forward in discussing animal food. Vegetables which are rich in proteins have the advantage of binding a great deal of acid, prolonging thus the amylolytic period of digestion, and thereby furthering the digestion of their carbohydrate constituents. Particularly rich in proteins are the so-called legumins, peas, beans, lentils, but they must be given in the form of well-cooked purées. There are in the market fine flours made of the dried legumins (for example, Knorr's Flour), which make up fine purées, or, when somewhat more diluted with water, can be taken in the form of thick soups. In cases with pronounced irritability (as in gastrosuccorrhea, gastric ulcer, etc.), which require a prolonged period of restricted diet, we are in favor of adding to milk and eggs such purées or soups made of leguminous flours. Purée is the best form of preparation for all kinds of vegetables. It is poor advice to advocate long-continued mastication instead, because mastication reflexly provokes gastric secretion. When, however, vegetables are taken finely prepared, mashed or strained, they quickly take up a great deal of secretion and leave the stomach in short order. If necessary almost all vegetables can be puréed; spinach, green peas, carrots, lettuce, beet tops, beets, squash, lima beans, oyster plant, Jerusalem artichokes, chestnuts, etc. With a less strict diet some vegetables are much preferred when offered in natural form, but they should always be made very soft by thorough boiling; asparagus, top of cauliflower, celery, string beans, kale, French artichoke, sweet potatoes, etc. Some patients even stand well purées of turnips,

parsnips, boiled Bermuda onions, etc. Coarse vegetables such as corn, cabbage, and mushrooms should be forbidden. Tomatoes are too acid. The acidity also makes most fruits harmful even when stewed. Of raw fruits sweet grapes or bananas, which are not acid, are sometimes permissible in mild cases. As a rule, however, it is better to avoid these and all other raw fruits. Salads and other raw vegetable food, celery, radishes, olives, nuts and other substances difficult of solution, all articles of food containing hard material such as seeds, etc., should be prohibited. Schmidt's recent investigations have taught us that cooking dissolves to a certain degree the middle layers of pectin, hemicellulose, etc., which otherwise have to be dissolved by the gastric secretion. The more thoroughly cooked the vegetable, the less it taxes gastric secretion. Bickel has further stated that, just as with meat, cooking deprives vegetables of extractive substances, which were shown to act as very forcible exciting agents of gastric secretion when given to animals internally or hypodermically. By being thoroughly cooked and puréed vegetables lose therefore chemically as well as mechanically a good deal of their power of exciting gastric secretion.

Starchy Vegetables and Carbohydrates.—In regard to vegetables rich in starch (potato, rice) and the so-called cereals, much depends on the state in which starch digestion is found in the individual case. The regulation of the carbohydrate intake, particularly in the form of starchy foods, is the most difficult point in hyperacidity diet. It seems to us that the difficulties are not simply to be overcome by claiming that an amylaceous diet has a curative effect, arguing that hyperacidity is rare among Eastern people who live mainly on carbohydrates, and that, as Hemmeter has shown, the acidity of the secretion in carnivora can be diminished by feeding on a carbohydrate diet for a long time. First of all, it is only in a certain percentage of cases that hyperacidity develops from long-continued overindulgence in meats. Such patients should certainly be taught to reduce the quantity of meat not only absolutely, but also relatively, and in arranging for them a mixed diet a gradually increasing amount of starchy food should be added. However, such an attempt can only be undertaken during free intervals, when the secretory disorder has abated after successful treatment. As long as hyperacidity is present, and as long as the premature rise of acidity curtails the normal period during which starch digestion can continue in the stomach, starches should be prohibited. The more pronounced the disturbance the more completely and the longer should starches be excluded. This is especially necessary in all cases with stagnation of gastric secretion. Few subjects of hypersecretion are able to take bread or other starchy foods without experiencing a considerable access of discomfort. When in such cases, after a period of milk and egg diet, the acute symptoms have subsided and the general state of nutrition makes it desirable to add some carbohydrates, we prefer, as stated above,

to allow leguminous flours first. Should they prove distasteful or cause discomfort starchy foods may be carefully tried, only, however, in some special form which has been already partly digested: a gruel of oatmeal, a cereal soup, barley water, or very fine flours of cereals thoroughly gelatinized by boiling them with milk, which covers the dissolved starch and carries it along into the intestine. Even in this form they should be given only in moderate quantities, preferably in the morning and after having removed by lavage stagnating acid secretion. In not a few cases starchy foods prepared even in such careful ways are apt to cause discomfort and then we have to restrict the diet to milk, eggs, and leguminous flours until meat and green vegetables can be taken. In such cases all other kinds of starchy food (potatoes, rice, macaroni, cereals which are not thoroughly prepared) must be avoided altogether for long periods, not less all starchy desserts and particularly bread, which, even in the form of toast and rusks, is a pronounced provoker of gastric secretion and is invariably poorly tolerated. This is especially so in the group of cases described as amylaceous dyspepsia, usually caused by overindulgence in bread and showing a great impairment of starch digestion. Such people are better off if they keep away altogether from bread and starchy foods for long periods. On the whole, in milder types of the secretory disorder when a more liberal mixed diet is in place, the allowance of starchy foods should be regulated according to the state in which starch digestion is found on examination.

As amylolysis does not take place if hydrochloric acid is present beyond a certain concentration, the administration of carbohydrates in cases of hyperacidity would seem to be unscientific and aimless. That this deduction is erroneous—at least to a certain extent—is demonstrated by the experiments of Gruetzner, corroborated by the X-ray examinations of Kaufmann and Kienboeck. According to these investigators the food in the stomach does not become homogeneous; the food last taken gravitates to the center of the mass while that first ingested adheres to the stomach wall; the wall, in turn, to the ingesta by virtue of its peristaltic power. Stratification of the foodstuffs in the order in which they are ingested takes place, so that while the layers adjacent to the wall may be soaked with acid gastric juice the interior layers are not affected by it; so that the ptyalin digestion, which begins in the mouth, can be continued for hours in a hyperacid stomach, the median portion of which is free from hydrochloric acid.

The degree of impairment of starch digestion varies greatly in hyperacidity cases; the less starch digestion is interfered with, the more liberal we may be with allowance of starchy foods. But even with a liberal allowance it is best given only in moderate quantities thoroughly prepared and according to the following rules. In the majority of cases it is best to give the allowance of starchy foods with the first meal in the morning,

provided the fasting stomach is free from acid fluid; toast, rusk, zwieback, crackers, starch-free biscuits, a gruel of oatmeal, thoroughly boiled farina or rice. All starch should be dextrinized by dry heat or thoroughly gelatinized by moist heat. Whatever bread is allowed should be taken in the form of thin slices crisply baked in the oven, and it should always be well masticated. In this case prolonged mastication has the advantage that the starch is partly digested during the act of chewing, wherefore it is best to have the toast eaten dry, without any fluids, so that it may become thoroughly mixed with saliva.

Certain patients have the greatest annoyance from hyperacidity after breakfast, no matter what it consists of; in such cases the allowance of starchy foods should be given with the midday or evening meal instead: baked potato, potato purée, soft boiled rice, tapioca pulp, etc. One kind of farinaceous food should always be sufficient with one meal, so that if potatoes are taken toast should be avoided and vice versa. The selection of the special kind of farinaceous food depends on the individual tolerance; some people have great discomfort after eating potatoes, which for others are the best tolerated of the starchy foods. The total amount of starchy foods with a single meal and with all the meals of a day should not be too great and should only form the smaller percentage of a mixed diet.

Desserts.—Great restrictions should be put on desserts. Since Strauss and others found that dissolved carbohydrates (for instance, a solution of sugar) reduce gastric secretion, sweet desserts have been recommended as a suitable food in hyperacidity. Practical experience, however, teaches us that hyperacidity patients are particularly annoyed by heartburn, flatulency, and painful sensations after partaking of sweet desserts. Even plain sugar solution readily undergoes fermentation, when motor insufficiency is combined with the secretory disorder. The advice to give therapeutically in hyperacidity a solution of dextrose or extract of malt should be followed only in selected cases without gastric atony, and then with caution. It is further often necessary to restrict the quantity of sugar used for sweetening tea, cocoa, cereals, etc. Honey is sometimes well tolerated. The combination of sugar and starchy foods seems to be especially liable to bring on fermentation, gas distention and increased secretion, and it is therefore decidedly better to eliminate entirely from the dietary of hyperacidity patients such desserts as pastries, pies, rich cakes, puddings, etc. When desserts are much desired by the patient, those prepared without starches are recommended: custards, blancmange, soufflés, gelatins, chocolate junket, etc. Even these are better tolerated when prepared without much sugar. Some people find a good substitute in cream cheese, best taken with a few crackers or starch-free biscuits.

Condiments and Spices.—In cooking food, vegetables as well as animal food, much seasoning should be avoided, nor should the patient himself

add condiments and spices; mustard, pepper, ginger, curry, paprika, horseradish, sharp sauces, vinegar, etc., must be forbidden. As mentioned before, hyperacidity is often the result of a long-continued habit of adding great quantities of condiments, particularly table salt, to every kind of food. In France the complete withdrawal of table salt (déchlorition) is used as an effective treatment of hyperacidity, based on the results of A. Cahn's experiments, which showed that with a salt-free diet the secretion of gastric juice is greatly reduced. At all events excessive quantities of salt should be strictly forbidden.

Alcohol, Coffee, and Other Drinks.—As long as the disturbance is present no alcohol in any form should be taken. All alcoholic drinks are strong provokers of gastric secretion, particularly in concentrated form and when taken before meals (cocktails). With some wines it is the acid as well as the alcohol which irritates and so, when patients, after being cured of the ailment, desire again to have some wine with their meals, they should abstain from acid wines as well as from cider and similar acid fluids. Light beer or whisky is preferable, 1 part diluted with 7 to 8 parts of water, or non-acid wines, also best well diluted with water. No alcohol of greater strength should be permitted and no alcohol of any kind apart from meals.

Patients who are not accustomed to have spirits with their meals are far better off if they take only water. Whenever the secretory disorder is combined with motor disturbances (alimentary and continuous hypersecretion) the allowance of all kinds of fluids taken with meals should be restricted as far as possible. With undisturbed motor activity of the stomach, however, a moderate amount of fluid taken with or at the end of a meal may help to dilute the acid secretion. For this purpose plain water or water containing some alkali is useful, or one of the natural alkaline waters, by preference those with a small amount of CO_2, such as Vichy, Ems, Fachinger, Seltzer, Evian, Contrexéville, etc. Most people like to finish their meals with a warm drink. They can either take warm water or a weak infusion of Chinese or breakfast tea. Much in fashion again and well tolerated are aromatic teas, such as camomile or peppermint. Coffee (with and without caffein) should be strictly forbidden at all times. Tea is decidedly less irritating for gastric secretion than coffee, but only when prepared fresh and in a weak infusion. Many prefer cocoa, which, although more irritating than tea, is a good breakfast food, particularly bitter cocoa prepared partly with water and partly with milk.

Drugs.—The administration of drugs is usually described as having principally two objects, to reduce the amount of secretion and to neutralize whatever superfluous acid is present. In discussing the different remedies we shall find, exactly as we found with the different food types, that the so-called "palliative" treatment of neutralizing the obnoxious acid often answers the first "causal" indication of preventing further secretion.

We shall further find a third not less important object of medication in the benefit derived from the increased secretion of mucus, which follows the use of certain remedies.

Atropin.—The remedy which is generally considered the most powerful in reducing gastric secretion is atropin, first recommended for the purpose by Riegel. Experimentally it was shown (von Aldor, Schiff, Lientier) to have an inhibitory effect on the pneumogastric nerve, the secretory nerve of the stomach. Opinions about its practical usefulness in hyperacidity are still divided. Some modern observers praise its prompt and reliable influence in most cases of secretory disorder (Tabora), while others claim that they have never seen gastric secretion reduced when using atropin alone without further treatment (Elsner). Fenwick states that atropin does not really diminish acidity and that, on the other hand, it not infrequently induces vomiting. Personally we have found that it exerts its inhibitive influence on gastric secretion principally in those cases which present symptoms of irritation of the vagus nerve, as hypersecretio nicotinica, acute attacks of intermittent hypersecretion, and the condition lately described by Eppinger and Hess as vagotony. We are not convinced, however, that its effect can be relied upon in all the different forms of irritative gastric disorder. In milder forms of hyperacidity, which usually yield to other methods of treatment, the drug is hardly recommendable on account of the disagreeable by-effects (dryness of mouth, disturbance of vision, etc.), which rarely fail to appear when atropin is properly given in doses which guarantee its full action. On the other hand, in the severe forms of hypersecretion we have found, like Fenwick, that it sometimes increases the vomiting. We admit, however, that in the severe forms of hypersecretion the condition is usually of such character that we employ simultaneously other means to stop the secretory irritation, which makes it difficult to decide what acts beneficially and what harmfully. Still we consider it advisable to try atropin in all cases of severe type, when pains and persistent vomiting call for all available help. Aside from reducing gastric secretion atropin relieves pylorospasm, which is usually associated with severe forms of hypersecretion. Whenever feasible it is preferable to administer it hypodermically, 0.5 to 1 mg. (1 to 120 to 1 to 60 gr.) two to three times a day. In ambulatory cases it should be given internally, either in tablet form or better in solution [10 to 20 drops of a solution of atropin 0.01 : 10.0 gm. (1 to 6 gr. to 2½ dr.) of water]. Tabora, who emphatically advocates its systematic use in all cases of pronounced hypersecretion, recommends that such doses be taken regularly for a period of two or three weeks and longer, provided the first few doses yield a favorable result. Individual intolerance will be observed immediately and should prevent the further use of the drug.

Belladonna.—Belladonna is frequently administered as a milder substitute for atropin. The extract of belladonna is the usual preparation, in

doses of 0.01 to 0.02 or 0.03 gm. (1 to 6 to 1 to 3 or 1 to 2 gr.) three to four times a day, either in tablet form by mouth or in suppositories in somewhat larger doses. Extract of belladonna is often added to different alkaline powders. The separate administration has the advantage of allowing more exact dosage, which can easily be changed or stopped altogether, according to needs, while the alkaline powders are continued.

Eumydrin.—Another substitute for atropin is eumydrin, recommended by Haas in doses of 1 to 2 or 4 mg. (1 to 60 to 1 to 30 or 1 to 15 gr.) three or four times a day, in solution, pills, powder, or suppositories.

Atropin and belladonna, when given in the usual dosage, according to the investigations of Tumpowsky, Crohn and Rehfuss, have no inhibitory effect, either on the secretion or on the motor function. Only such maximal doses as are not permissible for any length of time because of the risk of intoxication can affect continuous hypersecretion in the period after digestion and in pylorospasm. During the digestive period atropin may even increase the acidity and the secretion (Bastedo). Rehfuss attributes the inhibitory effect of the maximal dosage to the influence of psychic secretion.

Despite these interesting and striking results, this experimental explanation cannot be accepted as a basis for therapeutic procedure, because the results obtained at the bedside contradict these experimental findings. Just as the empirical administration of soda proves efficacious and justifiable contrary to the results produced by experimentation, here also the clinical efficacy of these drugs cannot find any experimental explanation. Nevertheless they are both useful, and we do not possess a more effectual means of combating hyperacidity, hypersecretion or ulcer. If they cannot influence the secretory and motor disturbances, they certainly can abate the sensory, that is, the neurotic component, which constitutes another argument serving to explain the disassociated, coördinate coexistence of both secretory and sensory disturbances.

Bismuth.—Next to atropin the drug most relied upon for reducing gastric secretion is bismuth. Since Fleiner and later Schüle described its retarding effect on gastric secretion it has been more and more extensively used for the purpose. Others (Cheinisse, etc.) attribute the undoubted relief following the administration of bismuth to its stimulating action on the secretion of mucus, which could be demonstrated experimentally (Matthes). In cases of amyxia, with and without hyperacidity, the effect of bismuth proves particularly beneficial in at once stimulating the secretion of mucus and retarding the glandular secretion. This justifies the extensive use of this drug in all cases of irritative secretory disorders of the stomach.

Different bismuth salts are in use: the subnitrate, the subcarbonate, the subgallate, and the bismuth tannate, preference being given to the one or the other by different authors. We side with those who consider the

subnitrate the most reliable. It yields the best results when given in doses of ½ to 1 teaspoonful on a fasting stomach and before meals. It can also be given advantageously in combination with different alkalis.

Alkalis.—Alkalis are the great standby for most sufferers from hyperacidity, which is readily understood when we consider that they usually afford immediate relief when taken at the time of discomfort and pain. In spite of the great comfort they offer to the patients, many practitioners counsel against the liberal use of alkalis. They argue that by neutralizing the excess of acid the alkalis give only temporary relief, which is followed by a renewed increase of secretion, caused by the irritating effect of the resulting salts. This is said particularly of bicarbonate of soda, which with HCl forms NaCl and CO_2, both of which are stimulating agents of secretion. While thus acting symptomatically the alkalis are said to have no curative effect, which would account for the fact that so many hyperacidity patients continue using alkalis for years and come to rely upon their neutralizing action if they want to feel comfortable. Not a few of these sufferers are never without their alkaline powder, which they always carry with them. It seems to us, however, that in many of these cases the persistence of the secretory disorder is not so much due to the steady use of the alkalis as to a continuation of the original cause of the hyperacidity. One of our patients for over forty years took religiously every day about 6 teaspoonfuls of bicarbonate of soda, averaging between 2 and 3 pounds per month. He was a very intense worker, at the same time a very hearty eater, particularly fond of all sorts of delicacies and liquors, usually winding up the day's toil by drinking 3 to 4 quarts of beer. He maintained that the conscientious use of bicarbonate of sodium taken on a fasting stomach, after each meal, and before retiring, enabled him to work persistently without being unduly annoyed by gastric discomfort, while at the same time indulging to his heart's content in whatever he was fond of having on his table and plenty of it. And so it is with many, to whom the relief afforded by alkalis gives the pretext to perpetuate their errors in diet and life. With properly arranged diet and mode of living, however, more than a mere symptomatic effect results from the use of alkalis, and we consider it an open question whether alkalis in general (if we except bicarbonate of soda) secondarily increase gastric secretion. Experimentally it has been demonstrated (Pawlow, Bickel, Heinsheimer) that alkalis when taken on an empty stomach reduce gastric secretion partly by direct action on the mucous membrane, partly by reflex action from the duodenum. This is the reason that some authors give for advising that alkalis be taken before meals in order to insure their full effect. We must not forget, however, that hyperacidity is a pathological condition which often requires different action. The suffering caused by hyperacidity necessitates the administration of alkalis at the time when the discomfort becomes annoying. Even when taken at such times after meals alkalis do more than stop

the pain by neutralizing the acid. In hyperacidity with a hypersensitive mucous membrane the free acid itself is a most pronounced irritant to gastric secretion, and by checking the free acid at the beginning of its appearance alkalis eliminate the irritant and act as sedatives, both by lowering the maximum of the acidity and by shortening the duration of the secretory disorder. Furthermore, in hypersecretion, particularly when pylorospasm retards the evacuation of the viscus, the spasm ceases with the neutralizing of the acid and in accomplishing a quicker egress of the stagnating contents the alkalis remove the real exciting agent of continued secretion. This shows that alkalis have not only a symptomatic, but a decided curative effect, even when given at the height of the discomfort for symptomatic purposes. For this reason we favor the liberal use of alkalis, whenever the subjective symptoms require them, at regular hours after meals, and repeated with returning discomfort, which is often necessary during the night in cases of severe character. As a rule we have to find out for each individual case the most appropriate time for the administration of the alkalis: one, two, or three hours after meals, respectively. In the cases of so-called larval hyperacidity, in which hyperchlorhydria is present during the earlier periods of digestion, the best results are obtained when alkalis are given directly after meals. When the suffering subsides alkalis may be given for curative purposes before or with meals. This may also be accomplished during the more acute stages, in addition to the above methods, particularly by giving alkaline waters before meals. Bickel, Sasaki, Rheinbold, and others have conclusively demonstrated that the natural alkaline waters of Carlsbad, Marienbad, Vichy, Tarasp, and other places decidedly reduce gastric secretion. This makes them very valuable in hyperacidity and justifies their systematic employment either at home or at the spa itself. Which place is best suited has to be considered for each individual case and depends to a certain degree on the general condition of the patient and on the condition of his bowels. The result gained in suitable cases at these places is sometimes very striking. Very good results are also obtained by having these waters taken at home for weeks and months. We know of patients who have for years taken a glass of hot Carlsbad or Vichy water in the morning before breakfast with great benefit.

In cases of constipation saline aperients may be added to the mineral water or taken in plain water before breakfast: phosphate of sodium, sulphate of sodium, sulphate of magnesium, etc. These salts can also be added to the alkaline mixture, taken before or after other meals. We have found, however, that strong salt solutions have an irritant effect on the stomach in certain cases and we then prefer to add a vegetable cathartic (rhubarb, etc.) to the alkaline powder, if the latter itself is not sufficient to regulate the bowels, which is frequently the case. The array of alkalis used in hyperacidity is great and they may be combined in many different

ways. Bicarbonate of sodium is by far the most effective and should be given when a quick result is desired. It has the disadvantage of producing CO_2, which not only stimulates secretion, but often annoys the patient by causing painful gas distention, relieved only by belching, which is objectionable to most patients. While this disadvantage is less marked when forming part of a mixture of different alkalis, it is being more and more replaced by citrate of sodium and biborate of sodium. We have also the different calcium preparations (calcium carbonate and tribasic phosphate), principally used when a tendency to diarrhea exists. In cases of constipation we prefer magnesia preparations: calcined magnesia, ammoniomagnesium phosphate, magnesia perhydrol. Lately we have used extensively magnesia perhydrol in doses of 1, 2 to 3 gm. (15, 30 to 45 gr.) with very good results. Investigations in von Leube's clinic by Poly showed that magnesia perhydrol exerts its beneficial effect principally by stimulating the secretion of mucus. Poly furthermore demonstrated both experimentally and clinically that another peroxid, the hydrogen peroxid first recommended by Petri, also acts beneficially in hyperacidity by producing more mucus. Hydrogen peroxid was administered in ½ per cent watery solution, 300 c.c. being given on a fasting stomach every other day and repeated in mild cases five times, in severe cases about ten times. The magnesia perhydrol seems the most practical preparation.

In choosing and combining the different alkalis we should always consider their effect on the bowels and on the secretion of mucus. We mentioned before that the value of bismuth is attributable to its power of increasing the secretion of mucus, which makes it a very useful constituent of alkaline mixtures.

The doses should be regulated according to the degree of the disturbance; severe disturbances require not only more frequent, but also larger doses. Of the magnesia preparations (particularly of the calcined magnesia) much smaller quantities are necessary to neutralize equal amounts of HCl than of sodium preparations. One gm. (15 gr.) of calcined magnesia is equivalent to 4 gm. (1 dr.) of bicarbonate of soda.

To all such alkaline mixtures may be added belladonna or codein when hyperesthesia or great pain requires sedatives. As with belladonna we prefer to give codein in doses of 0.02 to 0.06 gm. (⅓ to 1 gr.) separately for reasons given above. Morphin should be prohibited in chronic cases. In acute cases it is sometimes indispensable. Bromids, highly recommended by Steele as sedatives against hyperesthesia, are better administered by rectum.

The empirical value of the administration of hydrochloric acid in cases of achlorhydria, and of alkalis in cases of hyperchlorhydria or hypersecretion, cannot—at least in a good many instances—be denied. And the reason for their usefulness—though this statement may in itself seem contradictory—is less understandable in the light of the following reasons:

Under normal circumstances the quantity of gastric juice secreted in twenty-four hours is about 1,500 c.c. (Tigerstedt); the quantity of food and fluid taken in twenty-four hours can be figured on an average of at least 2,000 gm. and so the volume of ingesta altogether amounts to about 3,500 gm. (8 pounds) per day. Calculating the average normal total acidity of the stomach contents at 50, that is, 0.5 by 1/10 n.HCl, the average quantity of HCl secreted in twenty-four hours: 0.5 by 1/10 36 by 3.5 = 1.8. 3.5 = 6.3 gm. Acidum hydrochloricum dilutum, the drug usually administered in cases of achlorhydria, contains only 12.5 per cent HCl, and the usual dosage given is 15 drops (diluted in water) at a dose, 30 to 60 drops per day (Poulsson). The average dosage given in twenty-four hours amounts to 45 drops, which equals 3 gm. of the diluted, or 0.375 gm. of the pure HCl. In practice, therefore, instead of the full dosage of 6.3 gm., only 0.375 gm., or about one-twentieth of it, is actually administered. The same consideration reveals that for neutralizing one gram-molecule of HCl, one gram-molecule of sodium bicarbonate is necessary: 36 gm. of HCl require 74 gm. $NaHCO_3$ for neutralization.

In a case of hyperchlorhydria in which the hydrochloric concentration is but double its normal value, in order to neutralize the superfluous HCl, that is, to bring the hydrochloric concentration back to the normal, 12.5 gm. soda should be used. In a higher degree of hyperchlorhydria, especially in cases of hypersecretion, correspondingly higher doses will be required. When we take into account the relatively low average dosage of soda, which is given usually for the relief of hyperchlorhydric complaints, it is evident that it is the multiples which should be used in order to achieve a proper chemical neutralization. This disproportion is not so great as when HCl is administered in conditions of anacidity; it is, however, pronounced enough.

Hydrochloric acid and sodium bicarbonate given orally not only act as neutralizing agents, but also as stimulants to the secretory glands. The stomach glands possess a regulating power which maintains at about the same point the acid concentration characteristic of each individual. This power does not fail even when HCl or $NaHCO_3$ is administered. Galambos in his experiments made about fourteen years ago found that in both health and disease when high dosage of HCl or $NaHCO_3$ (not the usual therapeutic doses, but their multiples) was given during or immediately after the Ewald's test meal, the ingesta obtained sixty or ninety minutes later had about the same concentration as when no drugs had been ingested. This could not be explained except on the ground that the administration of HCl had a depressory effect; the $NaHCO_3$ taken had an irritative effect on the activity of the HCl-producing glands. The administration of hydrochloric acid lessen or even check the secretion of this acid, or if it failed—as in achlorhydria—it set up alkalinity, though whether this was accomplished by duodenal regurgitation, or by direct secretion of an

alkaline or possibly catarrhal fluid in the stomach, was not established. The administration of sodium bicarbonate increased the activity of the glands to such an extent that the presence of $NaHCO_3$ was counterbalanced by a corresponding increase in the quantity of HCl secreted. The results were strikingly unanimous. This property does not seem to be confined to HCl alone, for Tigerstedt mentions that the "addition of free acids (H_2SO_4, HNO_3) to the protein substances to be fed lessens the absolute quantity of the HCl secreted in a proportionate degree.

Bastedo's assertion fully conforms with this: "The value of alkalis is not to be measured by their power to neutralize acids." And this is further emphasized by the same author when he says, "Alkalis promote the secretion of acid in the digestive period." Both statements corroborate the findings of the author of these lines.

Bastedo says: "When giving HCl to avoid acidosis during the acid treatment, sodium bicarbonate should be given before breakfast and three or four hours after meals, giving enough to keep the urine just slightly acid."

There is also a third reason which makes it hard to understand the beneficial action of these drugs, especially that of the soda which is usually given after meals. Gruetzner's experiments, which have been extensively corroborated, undoubtedly show that, on account of the lack of homogeneity the foodstuffs last taken are propelled to the middle of the stomach, do not mix thoroughly with the rest of the stomach contents, and so can remain stratified there for hours. Soda, which is taken in powder form, after being slowly dissolved reaches the outside layers—where the neutralizing process is carried on by slow degrees and in a fractionated form.

The establishment of these facts satisfactorily proves that both kinds of medication, so extensively used in the therapeusis of gastric diseases, themselves offer a threefold reason why the mode of their activity cannot be explained on the ground of chemical neutralization alone. But as they actually do often prove useful in practice, a possible explanation of their efficacy may be found by referring to the theories particularly described in the chapter on Gastric Neuroses.

Some of our favorite formulæ are:

℞ Sodii bicarbonatis
Bismuthi subnitratis āā 15.0 ℥ss
Magnesii 10.0 ℨiiss
M. ft. pulv.
Sig. One-half to 1 teaspoonful in water one or two hours after meals.

℞ Sodii bicarbonatis
Rhei āā 15.0 ℥ss
Magnesii 10.0 ℨiiss
M. ft. pulv.
Sig. One-half to 1 teaspoonful in water at night.

℞ Magnesii 15.0 ℥ss
Elæosacch. menth. pip. 5.0 gr. lxx
M. ft. pulv.
Sig. One-half teaspoonful in water one hour after meals.

℞ Calcii phosphatis tribasic
Bismuthi subnitratis āā 15.0 ℥ss
M. ft. pulv.
Sig. One-half to 1 teaspoonful one hour after meals.

To quote some other formulæ:

℞ Magnesii 15.0 ℥ss
Sodii citratis 10.0 ℥iiss
Eumydrin 0.03 gr. ½
M. ft. pulv.
Sig. One teaspoonful 2 or 3 hours after meals (Zweig).

℞ Sodii bicarbonatis
Magnesii āā 10.0 ℥iiss
Ext. belladonnæ 0.15 gr. ii
M. ft. pulv.
Sig. One-half to 1 teaspoonful one hour after meals (Elsner).

℞ Magnesii carbonatis 10.0 ℥iiss
Sodii citratis 5.0 gr. lxxv
Codein. phosphatis 0.2 gr. iii
M. ft. pulv.
Sig. One-half teaspoonful one hour after meals (Elsner).

℞ Magnesii 20.0 ℥v
Sodii citratis 10.0 ℥iiss
Sodii sulphatis 5.0 gr. lxxv
(or magnesii sulphatis)
M. ft. pulv.
Sig. One-half teaspoonful before meals (Tabora).

℞ Ext. belladonnæ 0.5 gr. vii
Bismuthi tannatis 10.0 ℥iiss
Magnesii carbonatis
Sodii bicarbonatis āā 20.0 ℥v
M. ft. pulv.
Sig. One-half teaspoonful every two hours (Ewald).

Lately some aluminum preparations have been recommended in the treatment of irritative gastric disorders: escalin by George Klemperer, neutralon by Rosenheim, and kaolin (aluminum silicate, the old bolus alba), by Hemmeter. Their value has still to be established.

Lavage.—Lavage plays a great rôle in the treatment of irritative secretory disorders. The abuse of lavage by incompetent hands has somewhat discredited this valuable method of treatment. We consider it, however, a great mistake, on account of such abuse, to abandon lavage altogether in hyperacidity or to restrict it to the most urgent conditions, as is advised by some writers. Personally we would not readily give up the employment of lavage, which, when judiciously applied, has yielded better results in the treatment of patients than any other method of treatment that has come to our knowledge. Authors who counsel against lavage often argue that Kussmaul, when introducing this method, wanted it employed only for removing stagnating food in cases of gastric dilatation. As a former assistant of Kussmaul we can positively state that this is an erroneous conception of Kussmaul's ideas in regard to the usefulness and availability of gastric lavage. Our own experience at his clinic, as well as the publications of other pupils (Malbranc, Cahn, Fleiner, etc.), bear witness that Kussmaul made a very liberal use of lavage in all the different disturbances and diseases of the stomach, employing it in atonic conditions to raise the motor and secretory tonus of the organ, and again in irritative disorders to combat gastric intolerance and hyperesthesia. His own first article, published in 1867, already reports his method of using lavage as a vehicle for the application of certain drugs and remedies. Furthermore, the argument that lavage is indicated only when stagnation is present should certainly not exclude it in chronic hypersecretion, a condition which is characterized by the stagnation of acid secretion. In fact, the removal of this stagnating fluid forms the most essential part of the whole treatment. In cases of hypersecretion no other remedy (except surgical interference in given cases) compares in efficiency with lavage, no other treatment relieves pain and vomiting as quickly as the evacuation of the acid contents through the tube. In such cases lavage brings not only prompt and generally complete relief, but has also a decided curative effect. No other harmful influence proves more deleterious in this connection than the constant irritation of the gastric mucosa by the stagnating acid which perpetuates the disturbance. The removal of the acid fluid by lavage eliminates this most harmful influence, facilitates the evacuation of the stomach, and thus greatly reduces gastric secretion both in intensity and duration. In cases of pronounced hypersecretion, with severe pains occurring during the night, which are not sufficiently alleviated by alkalis, atropin, etc., it may become necessary to evacuate by lavage the acid contents of the stomach late in the evening. Patients who have learned to introduce the tube themselves obtain the quickest relief from the usually very severe night attacks by emptying the stomach by means of the tube. As a rule, however, it is far preferable to apply lavage in the morning before breakfast. Its beneficial effect upon the tolerance of the gastric mucosa will make itself felt for the rest of the day. We

employ for lavage a weak alkaline solution, 1 teaspoonful of bicarbonate of soda to 1 quart of warm water. The natural alkaline waters, like Vichy, Carlsbad, are very useful and beneficial but too expensive.

The beneficial effect of methodical lavage can be enhanced by using remedies which we are accustomed to apply in the treatment of mucous membranes of other organs, principally zinc sulphate and silver nitrate. We were able to demonstrate that these solutions act mainly through their stimulating effect on the secretion of mucus. The well-known beneficial effect of silver nitrate was formerly attributed to its power to reduce gastric secretion. Our own observations and those of others (Baibakoff) showed that silver nitrate does not necessarily reduce the secretion of gastric juice. In certain cases we found a decided lowering of the acidity after employing silver nitrate. But we have seen more cases in which the acidity remained high; in fact, in some the acidity was higher after treatment than before. And yet these patients were freed from their annoying symptoms by the use of silver nitrate and many of them were promptly relieved from severe pain. Examination of the stomach contents proved that the unmistakable change of tolerance of the mucous membrane to the irritating effect of the acid was accomplished by an increased secretion of mucus. This is particularly valuable in cases which show a lack of mucus (amyxorrhea), when the insufficient covering deprives the mucosa of its protection against the irritant influence of its own acid secretion. This is a condition which often accounts for hyperacidity symptoms in cases with normal or only slightly increased amounts of acid. The power of the silver nitrate to induce an increased secretion of mucus had been demonstrated in Pawlow's experiments. It can be turned to advantage as a therapeutic agent in all cases of gastric irritability in which the gastric mucosa is subjected to the irritating effect of its own acid secretion. This applies not only to cases of continuous hypersecretion or gastrosuccorrhea where lavage is indicated for the removal of stagnating acid fluids, but in the same manner to all irritative secretory disorders without stagnation, to plain hyperacidity, etc. The indication for this treatment is based much more upon the degree of the subjective suffering than upon the objective findings of gastric analysis. When people suffer from severe discomfort and pain they are entitled to the benefits of this treatment, even when gastric analysis shows moderate hyperacidity without stagnation. On the strength of an experience gained by the treatment of many hundreds of cases we can positively state that no treatment more quickly removes all the so-called hyperacidity symptoms than the application by lavage of solutions of zinc sulphate and silver nitrate.

Many of our patients who for some reason or other periodically have attacks of hyperacidity report at the outset for treatment, knowing by experience that when applied at an early period a few applications are often sufficient to reduce quickly the irritability and intolerance of the

stomach and that afterwards the treatment by diet and medication yields prompter and better results. When the introduction of the tube is not feasible silver nitrate may be given by mouth, 1 tablespoonful of a solution of 0.2 : 100.0, three times a day before meals. The probability of argyrosis prohibits its continuation for long periods. The application by the stomach tube permits the removal of the silver after its action and thereby makes it possible to employ much larger quantities. For the same reason this method of application is preferable to others, for example, by spray as recommended by Einhorn, the more so since the spray apparatus also has to be introduced into the stomach. The silver solution is best applied after a short washing with an alkaline solution; the latter is also used to remove the silver after it has remained in the stomach for a few seconds to one minute. We long ago gave up the sodium chlorid solution, which is usually recommended for washing out the silver nitrate, because we found the sodium chlorid solution very apt to produce nausea and vomiting, which is avoided by using an alkaline solution. When applied through the tube about 300 c.c. are given of a solution of 1 : 5,000, gradually increasing to 1 : 1,000. Zinc sulphate is given in the same quantity and concentration. It acts in the same way as the silver, only in a milder degree. As a rule we start the treatment with the weaker zinc sulphate solution, which often suffices to alleviate the condition; if not, it is followed up by the silver treatment. In order to have the solutions come into thorough contact with the mucous membrane it is necessary to apply them on an empty stomach. The best time is in the morning before breakfast. When conditions make it preferable to have the treatment before the other meals, a lengthy interval after the previous meal should be allowed in order that the stomach may be empty. The number of treatments depends partly on the severity of the condition, partly on the individual tolerance. With certain patients it is the hyperesthesia, either of primary neurotic origin or the result of continued hyperacidity, which produces the pain or discomfort on the mere contact of food. In such cases a few treatments are frequently sufficient to alleviate the hyperesthesia. In other cases with more pronounced disorders, and particularly when associated with organic changes (gastritis acida, gastrosuccorrhea, etc.), more is required than relief for the moment only. If an attempt is to be made to remedy the condition of the mucous membrane and change its faulty tendencies to secretory disorder, persistent treatment is in order. It may be necessary for a while to give the treatment daily, later, with improved condition, every other day, gradually prolonging the interval, yet continuing the treatment once a week for a considerable period. The subjective feeling of the patient is always a good guide for regulating the duration of the treatment.

Finally, we give some physical methods employed in hyperacidity.

Hydrotherapy.—Of hydrotherapeutic measures wet compresses around the abdomen, especially the so-called Priessnitz compress, when ap-

plied at night often diminish the irritability of the stomach by relieving the congestion of the organ. Severe pain requires hot applications, hot compresses, or hot-water bags. In chronic cases with persistently recurring pains the methodical application of flaxseed or mud poultices proves very helpful. Their place may be taken by the electric pad when the facilities of the house permit its use.

Electricity.—Electricity has been recommended in different forms. Our method is anodization of the vagus in the neck to reduce the irritability of this nerve in cases where this plays a prominent rôle in the disturbance. Here in this country intragastric galvanization and faradization have found many followers since Einhorn and others praised their usefulness. In recent years high frequency currents have been more exploited in the treatment of hyperacidity. Opinions in regard to the value of all these methods are divided.

Summary of Conditions in Which Hyperacidity and Hypersecretion Are Observed

The principal methods of treatment have been more fully discussed because of their greater reliability in all the different forms of irritative secretory disorder. To what extent they should come into play depends on two factors: (1) on the degree of the disturbance as shown in the objective findings; and (2) on the amount of subjective suffering. The two factors by no means run parallel. We find great suffering with mild degrees of hyperacidity and should advise in such cases the stricter forms of treatment, ordinarily employed in the more severe forms of secretory disturbance. In giving a summary of the conditions in which hyperacidity and hypersecretion are observed, we do well to keep this in mind.

Hyperacidity and Diet.—In not a few cases it is sufficient to eliminate errors in diet and mode of life. When not possible or sufficient, alkalis should be given and a mixed diet arranged, consisting principally of albuminous food, vegetables, and fat, excluding starches according to the state of starch digestion. Patients who habitually suffer from hyperacidity should adhere to the form of diet which proves most suitable; others require dieting only during an attack.

With severe suffering a strict milk diet may be advisable for a number of days. Codein and belladonna should be prescribed according to needs. Very annoying symptoms call further for lavage with zinc and silver solutions and eventually for the use of oil before meals.

Amyxorrhea (Amyxia) Gastrica.—The latter methods are particularly indicated when lack of mucus is the essential feature. In this condition of amyxorrhea the lack of mucus (with or without hyperacidity or hypersecretion) accounts for the hyperesthesia which is greatly ameliorated by the increase of mucus following the application of zinc and silver

solutions. For the same reason other remedies known to increase the secretion of mucus are especially indicated: bismuth, magnesia perhydrol, hydrogen peroxid, etc.

Careful attention should be paid to causative derangements of the nervous system and other etiological factors. When hyperesthesia is caused by anemia iron preparations are in order and helpful, but they are poorly tolerated in ordinary cases of hyperacidity.

Gastritis Acida.—Here hyperacidity is associated with an increased amount of mucus containing cellular elements, which indicates a pathological change in the gastric mucosa. Since this form often leads to the development of atrophic gastritis every effort should be made to remedy the condition by local treatment. This is best accomplished by lavage or by the methodical use of alkaline waters at home or at the spa (Carlsbad, etc.), by the employment of alkalis after meals, by strict dieting along the lines described above, which should be adhered to for long periods, in order to avoid recurrences and to give the mucosa a chance to return to a more normal condition.

We have now to consider secretory disorders when they are associated with motor disturbances.

Hyperacidity with Hypermotility.—When alkalis prove ineffective hydrochloric acid may be tentatively administered with or after meals, conforming with Best and Cohnheim's suggestion. They argue that in these cases hypermotility is the direct cause of hyperacidity, inasmuch as the rapid evacuation of the stomach brings about a high percentage of acids in the comparatively small amount of remaining contents. Hydrochloric acid may have a good effect in regulating the rhythmic activity of the pylorus and antrum pylori, which is lacking and is the actual cause of the hypermotility. The subjective feeling of the patient will immediately tell whether hydrochloric acid has the desired effect of retarding the evacuation and thereby preventing the formation of hyperacidity. If it does not relieve the annoying symptoms of hyperacidity it should be discontinued and alkalis given instead.

Alimentary Hypersecretion.—While the treatment is that of hyperacidity in general, special attention should be paid to the gastric atony, which is the characteristic feature of this group of cases. The atony permits the accumulation of the increased secretion. Food should be selected and prepared with a view of having it pass through the stomach in the shortest possible time. For details the reader is referred to our discussion of dieting given above, but we must discuss the question of fluids here. As a rule it is better to avoid adding fluids without nutritive value to meals, such as water, tea, etc., because they unnecessarily increase the total amount of a meal. There is, however, no objection to giving meals of fluid food of high nutritive value such as milk, leguminous soups, etc., which have the advantage of quickly leaving the stomach. As a rule these

patients are asthenic and underfed, and while it is well to avoid overloading the stomach with a given meal, yet a sufficient amount of carefully selected and prepared food should be given to raise the state of nutrition, which in turn will raise the gastric tonus. A methodical rest cure is often the best form of treatment and should be furthered by hydrotherapeutic measures, massage, and faradization of the abdomen, in fact, by all the methods which will be described for the treatment of gastric atony. Measures intended to reduce gastric secretion directly (atropin, alkalis, etc.) have much less effect here.

Acute or Intermittent Hypersecretion.—Acute or intermittent hypersecretion coming on in attacks of severe pain and violent vomiting, lasting a few hours or days, may be an early phase or acute exacerbation of chronic hypersecretion, and should then be treated accordingly. When occurring with an otherwise normal stomach it may be caused by overexcitement, fatigue, or tobacco poisoning. It may precede or follow the menstrual period, appear in the form of a gastric crisis of locomotor ataxia, as a syndrome of cerebral tumor, as a postoperative syndrome, and in children as paroxysmal vomiting, probably due to metabolic disturbances.

Between the attacks the individual underlying cause should be made the object of treatment; faulty habits in eating corrected (children); excessive smoking and drinking forbidden; mental overstrain and overworking avoided; all derangements of the nervous system, the pelvic organs, etc., attended to.

During the attack the quickest way of relieving the pain and vomiting is lavage with a weak alkaline solution, repeated several times every four to six hours. If lavage is not possible, alkalis (bismuth, magnesia) should be freely administered every few hours to neutralize the excessive acid. In some cases frequent drinking of moderate quantities of hot (alkaline) water relieves the great strain of retching and vomiting; in others this is accomplished by atropin injections or belladonna suppositories. When all these measures fail morphin injections may become necessary to stop the excessive vomiting and excruciating pains, particularly in cases of locomotor ataxia, cerebral tumor, and other organic affections. In the majority of cases the suggestion of food is impossible and altogether inadvisable. In some cases, however, with an attack running over several days, small quantities of milk with Vichy or limewater, albumin water, or grated hard-boiled eggs are tolerated. After the attack the diet should always be restricted for a few days to milk and eggs before the patient gradually returns to his ordinary diet.

Continuous Hypersecretion (*Gastrosuccorrhea; Reichmann's Disease.*)—This condition, chiefly characterized by the presence in the fasting stomach of acid secretion is observed in patients suffering from more or less severe gastric pains coming on regularly several hours after meals, and particularly during the night, and usually associated with vomiting of

highly acid matter, often of severe character. Ever since Reichmann, in 1882, first described gastrosuccorrhea, an extensive and lively discussion has been going on in regard to the nature of the disturbance, a discussion which is very active at present and which we have to take up briefly, because the treatment depends entirely on the conception which one forms of the pathogenesis of the disturbance. It was the opinion of Reichmann and his followers that the disturbance was in the main a secretory perversion of nervous origin. They explained the presence of acid fluid in the fasting stomach by the fact that the irritative secretory disorder caused a continuation of secretion not only during meals, but also during the intervals when the stomach of a normal individual should be empty. Subsequent investigations showed that increased secretion alone was not sufficient explanation for the clinical picture. The presence of acid fluid in the fasting stomach invariably means stagnation, caused either by spastic or organic obstruction at the pylorus. The writer took part in demonstrating that the clinical picture of continuous hypersecretion meant a motor as well as a secretory disorder, and at present it is generally held that the motor disturbance at the outlet of the stomach is an essential part of the condition.

Indication for Operative Treatment.—This conception of the rôle which the pylorospasm plays in the development of the syndrome is responsible for the advice so frequently given to perform gastro-enterostomy in such cases if they do not yield readily to medical treatment.

Formerly we were ardent advocates of early operative treatment, particularly because we were convinced, like so many others, that gastric and duodenal ulcers are frequently present in cases of gastrosuccorrhea. Lately we have become more conservative in advising gastroenterostomy, since we have had patients return to us with renewed gastric disorders after a period of freedom from discomfort, which impressed the surgeon as having effected a cure. We had to realize that pylorospasm, while an important part of the condition, is only a part of it, and that the secretory disorder must not be underestimated.

Hypersecretion and pylorospasm are closely interlinked; both are at the same time cause and effect of each other. In not a few cases both phenomena are simultaneously provoked by irritation of the vagus nerve, either as a manifestation of an inborn disposition (lately described by Eppinger and Hess as vagotony) or by chronic intoxication (tobacco, etc.), or by reflex action from various centers of irritation. At present there is a tendency to consider, next to gastric and duodenal ulcer, chronic appendicitis and gall-stones as the most frequent centers of irritation and causes of the irritative gastric disorder. This view, which is based on findings at operation, is held by many eminent surgeons, particularly by William Mayo in this country and by Paterson in England. The facts are undoubtedly correct; the problem, however, which is still to

be solved is given in the question, What is cause and what is effect? Opinions regarding gastric and duodenal ulcer have already undergone a change. Formerly considered the most common cause of continuous hypersecretion, they are now described as a result of this disorder. We quote Fenwick who, among medical men, is the most emphatic exponent of the theory "that chronic hypersecretion is not a disease, but merely an expression of an organic lesion of some part of the digestive tract or of those organs that pour their secretions into it." He states that "whatever be the immediate cause of the hypersecretion the continued existence of the latter not only excites inflammation of the stomach and duodenum, but also produces hemorrhagic erosions, which occasionally increase in size and depth and finally acquire all the characteristic features of chronic ulcers. In this manner both gastric and duodenal ulcers are apt to ensue from hypersecretion due in the first instance to gall-stones and appendicitis, while the chronic colitis that develops in so many cases of hypersecretion may eventually lead to inflammation of the appendix." The last part of the sentence shows that Fenwick is inclined to reverse the order not only for gastric and duodenal ulcer, but also for appendicitis. Thus he considers under certain conditions hypersecretion as the cause and appendicitis as its sequel—a view which we fully endorse. Some years ago the author pointed out that hyperacidity and hypersecretion, while often caused by gall-stones, may themselves provoke cholecystitis and gall-stone attacks. Undoubtedly there is a close connection between these various anatomical lesions and the continuous hypersecretion of gastric juice. The question is what is the primary, what the secondary disturbance. With hypersecretion and an anatomical lesion once developed a vicious circle is formed which makes it difficult to answer this question. The finding of the lesion at operation is not sufficient proof that it is the primary factor. We are convinced that the further study of these conditions, particularly in the earlier stages of their development, will demonstrate that in the majority of cases the inborn or acquired disposition to irritative gastric disorders is the primary factor. Taking this view we cannot conceive that surgical interference is an essentially causative treatment of continuous hypersecretion. It is true that during the later stages of the condition the removal of a diseased appendix or a diseased gall-bladder may prove very effective treatment, particularly in those cases where the irritation emanating from these centers has become the predominant feature, the elimination of which breaks the vicious circle. Some patients derive a lasting benefit from such operations provided that there is no other center of irritation and that the original underlying cause, the irritability of the vagus nerve, etc., has subsided. In many cases, however, the underlying causes, the inborn or acquired irritability of the vagus nerve and the tendency to irritative gastric disorders, remain unchanged by the removal of the gall-bladder

or the appendix, and they are apt to create renewed symptoms when provoked from some other center of irritation, already existing or developing after the operation. If these patients want to remain free from trouble they have to undergo medical treatment for the irritative gastric disorder after the operation and eventually follow it for a long period of time. Now, if these patients submit to a thorough and persistent medical treatment from the beginning, good and lasting results are often obtained and many a contemplated operation becomes unnecessary.

With growing experience we become more and more inclined first thoroughly to try medical treatment along the lines already discussed. We are still in favor of operative treatment when chronic appendicitis or cholecystitis give enough trouble on their own account to warrant surgical interference. And, further, we are still in favor of operations on the stomach in those cases of continuous hypersecretion associated with gastric and duodenal ulcer which do not yield to medical treatment, which have become intractable (cicatricial, pyloric obstruction, etc.), or when the circumstances do not permit of a long-continued dietetic and medical treatment. With patients of the laboring class the indication for operative treatment comes sooner than with patients who are in a position to continue the dietetic and medical treatment for a long period of time. In no case have we seen harm result from a thorough and long-continued medical treatment. If, on the contrary, such patients finally come to be operated, they are better prepared for it and derive better results. One condition, however, should be clearly understood, that is, that the medical treatment be controlled by a physician experienced in the handling of such cases.

It is generally stated that certain operations, that is, gastro-enterostomy, yield far better results when done by experienced operators than when done by others. Lockwood figures the mortality in uncomplicated gastro-enterostomy performed by a skilled surgeon at from 2 to 3 per cent, by the average surgeon 6 to 8 per cent. We claim a greater difference in the results of medical treatment when directed by the experienced specialist and the general practitioner respectively. The greater experience will prevent the specialist from dallying too long with medical treatment in cases which require operation. He will be able to judge whether his patient is yielding to a carefully laid out treatment with a fair prospect of ultimate recovery, or whether he is dealing with a case which is not amenable to his methods on account of anatomical alterations which call for surgical proceedings. The determination of a proper indication for operative treatment is essentially within the domain of the internist. Certainly he must know the limitations of his methods of treatment, and after carefully weighing the pros and cons in each individual case should not hesitate to hand the patient over to the surgeon when he becomes convinced that his methods do not avail. Yet, while it is certainly unjustifi-

able to continue unsuccessful medical treatment beyond a reasonable period of time, it is, on the other hand, just as unjustifiable not to give the patient a fair chance to get rid of his trouble by following conscientiously a strict and prolonged medical treatment. There is still a certain percentage of mortality connected with the operation, and those who recover from the operation are by no means all permanently cured. In those cases with a pronounced tendency to hypersecretion we should particularly keep in mind the danger of peptic ulcer developing in the jejunum after performing gastro-enterostomy—to mention only one of the many possibilities connected with operative treatment.

Medical Treatment.—The medical treatment of Reichmann's disease should be strictly enforced in every respect. It should, in the first place, make use of every method known to reduce gastric secretion. The condition represents the most severe type of irritative secretory disorder, complicated with pylorospasm, which greatly aggravates the disorder. In nearly all cases of this type gastric or duodenal ulcer is present, irrespective of the nature of the original cause of hypersecretion. The treatment is therefore based on the same principles as the ulcer-treatment, which best fulfills the most essential indication of setting the stomach and its secretion at rest; in fact, in gastrosuccorrhea we usually have to enforce a strict ulcer-treatment for longer periods than in uncomplicated ulcers on account of the complication with pylorospasm.

Whenever the patient can afford it he should stay in bed from two to six weeks. Securing complete rest of body and mind is the safest method of reducing gastric secretion when properly supported by strict dieting and medication. In aggravated cases it may be necessary to start with a few days of exclusive rectal feeding in order to give the stomach a complete rest. After this, or from the beginning, a strict milk diet is in order. Gastric lavage and the methodical use of zinc sulphate and silver nitrate solutions are essential. They should particularly be insisted upon with patients who cannot afford to stay in bed. In these conditions gastric lavage relieves the suffering quicker than any other method of treatment, by removing the irritating gastric secretion. Large doses of atropin should be given for several weeks, when possible hypodermically with patients staying in bed, otherwise internally. Liberal use should be made of bismuth and the different alkalis before meals, after meals, and whenever pain and discomfort call for amelioration. In many of these cases 1 or 2 tablespoonfuls of olive oil given before meals prove very beneficial.

This strict form of treatment should be kept up for several weeks, if possible. It is on the whole a difficult matter to law down exact rules and figures in regard to how long a patient should stay in bed, how long he should keep up lavage, how long he should continue the use of atropin, when he should change the diet, etc. It is wiser not to determine upon these points beforehand but to be guided by the symptoms and by the run

of the case. In any event it is best to proceed slowly. The longer the period of comparative rest the better the prospect of keeping the secretory disorder subdued. Before we can let up on the strict treatment the patient should have been entirely free from all discomfort for some time, the fasting stomach must contain no acid fluid, and the stools must be free from occult blood.

He must further remain free from all these symptoms when with a steady improvement we gradually drop the atropin and lavage, and carefully add to the diet list. Alkalis should always be continued for a long period of time. It is often very beneficial to give natural alkaline waters (Vichy, Carlsbad, etc.) methodically in the morning after lavage has been stopped, or, instead of lavage, when it is altogether omitted.

In regard to the Diet we should gradually add eggs, meat-free soups made of leguminous and similar flours, vegetable purées, etc., following the rules given in the above discussion on diet in hyperacidity, to which we must refer for details. The leading idea is to select food which is prepared in such a way that it quickly leaves the stomach without making much demand on secretion. We should always proceed slowly, trying one kind of food at a time and so finding out whether it agrees with the patient. With cases of long standing we prefer to have the patient stick to the milk-egg-leguminous soup diet for a long time. It is an erroneous idea that such a diet does not offer enough nutritive material. These patients are usually highly emaciated and the loss of weight is caused by the hypersecretion, by the pains, and most of all by the sleepless nights. As soon as all these symptoms disappear under the treatment described above such patients thrive even with a plain milk diet, so that we have seen them gain 20 and 25 pounds within a number of weeks.

As a rule we are dealing here with cases of long standing and it is essentially a question of persistency whether the improvement gained during the first period of strict treatment will be a lasting one. Among our present patients there is a physician who came to us eight months ago with all the symptoms of gastrosuccorrhea and from the first pronounced stagnation of food, indicating that there was probably more than a mere spastic obstruction of the pylorus. His own personal experience made him very chary in regard to gastro-enterostomy and he preferred to try a long-continued medical treatment, not minding how long it would take. With lavage, silver nitrate treatment, and the use of alkalis he lost all subjective and objective symptoms, and, although from the start attending to his practice, which keeps him active from morning till night, he has gained 25 pounds on a diet consisting of milk, eggs, leguminous flours, and vegetable purées, a diet to which he is only now occasionally adding chicken or fish. We could write of a long series of similar cases. When such people have the patience and persistence necessary to adhere to the diet and treatment laid out for them, and

have periods of more active treatment again when symptoms of irritation recur, they not only lose the symptoms of pyloric obstruction but the tendency to hypersecretion as well. Of course, there must be a pronounced tendency to steady improvement if we are to continue with medical treatment, otherwise we have to consider operative interference.

DEPRESSIVE DISORDERS OF GASTRIC SECRETION

We observe complete lack of gastric juice (achylia gastrica) or diminished secretion in various conditions. They are either the result of destructive changes in the gastric mucosa, caused by inflammatory or toxic processes (acute and chronic gastritis, carcinoma, pernicious anemia, etc.), or they appear as an independent functional disturbance. The latter form (achylia gastrica simplex) may be caused by deranged innervation, as first described by Einhorn, or it may represent a congenital constitutional shortcoming.

Achylia Gastrica, Anacidity, Hypo-acidity

Anacidity and hypo-acidity are similar conditions, the difference between them being quantitative only, in contradistinction to achylia gastrica, which is a disease sui generis. The principal difference between achylia and anacidity resides in the fact that when organic diseases are followed by achlorhydria, this is usually the anacidity and not the achylia, as in cases of cancer, gastritis, etc. Hernando and Alday found achylia only 3 times among 22 cases of anacidity accompanying gastric cancer. While anacidity is frequently only a symptom, achylia more often is an independent disease.

Chemical analysis and the appearance of the ingesta also confirm this principle of differentiation. In achylia both hydrochloric acid and pepsin are absent. The total acidity is likewise reduced to zero or it reaches a very low figure, like 2 or 3. In both anacidity and hypo-acidity pepsin is present and HCl is also secreted, but most of it is found in bound form, free HCl being lacking in anacidity and diminished in hypo-acidity. The total amount of acid is higher in anacidity than it is in achylia, varying about from 10 to 20. When anacidity is a symptom of a disease (cancer) which presents motor insufficiency, the total acidity may reach as high a figure as from 70 to 80, or even more, because of the presence of organic acids. Lactic acid is present as the resultant of anacidity and motor insufficiency, and furnishes an indirect but nevertheless significant sign of gastric cancer. A discussion of the typical appearance of the achylic gastric contents cannot be taken up here.

When dealing with the question of diminished secretion, it must be remembered that Rehfuss' fractional examination of the stomach contents may reveal errors in diagnosis of anacidity, in cases where delayed hyperacidity exists.

By means of Rehfuss' fractional examination of the stomach contents, after a special test meal has been ingested, we can examine single portions of the ingesta during the different stages of digestion. At fifteen-minute intervals about 10 c.c. are withdrawn by means of a syringe. While this method undoubtedly possesses advantages over the single tube test, the objections made by Gorham, Wheelom and Koppleman should, however, be borne in mind; they call our attention to the fact that the gastric chyme in itself is not a homogeneous mixture, so that different parts of the stomach contents may simultaneously vary in acidity and other chemical properties.

The principles of treatment regarding diet and medication are in many respects identical for the different forms and will therefore be discussed here in a general way, applicable to all the different conditions as far as the secretory disturbance is concerned. Further indications for treatment of inflammatory processes, carcinoma, etc., will be found under the respective headings.

The finding of the secretory disorder in itself does not necessitate the institution of treatment. Complete lack of gastric secretion, as found in cases of achylia gastrica simplex (Martius), is often remarkably well borne, particularly in the numerous cases in which the functional defect in all probability is an inborn constitutional shortcoming. In these cases the activity of the pancreas and the intestines makes up for the missing digestive activity of the stomach, often so perfectly that in spite of persistent achylia the patient is able to partake of all kinds of food without experiencing any discomfort and further to digest everything to such a degree as to keep in an excellent state of general nutrition. We have been thoroughly convinced of this in following up a large series of such cases over a number of years.

As long as these people feel well on an ordinary mixed diet, and this applies in the same manner to patients with subacidity, there is no reason whatsoever for putting them on a restricted diet or treating them in any other way. The constant attention going with strict dieting is liable to make them unnecessarily self-centered hypochondriacs. The lack of secretion becomes an object for treatment only when it causes gastric discomfort or, what happens frequently, when the compensatory activity of the intestines proves insufficient, and intestinal putrefaction of poorly digested food particles causes diarrhea and other disturbances.

During such periods of treatment the individual tolerance of the patient should be studied and he should be taught what errors in diet and mode of living to avoid in order to prevent the recurrence of disturbances.

If successfully carried out this plan will put many of these patients in condition to keep their digestive tracts and general nutrition in good shape in spite of continued lack of secretion. Some have to observe a more restricted diet than others, particularly during periods when the stress and strain of work and worry reduce their power of resistance. During and after the periods of treatment full use should be made of all the help which medication offers, always preferring those drugs which have proved particularly helpful in given cases. The individual tolerance varies greatly in regard to diet as well as to medication and should be fully considered. It will enable the patient to learn what is best suited to his individual case.

A condition which requires particular attention in all cases of diminished secretion is the motor activity of the stomach. Where it is normal the effect of the secretory disorder is easier counterbalanced by the compensatory activity of the intestines. With gastric atony and motor insufficiency the undigested stagnating masses irritate the stomach mechanically and chemically by products of fermentation and further irritate the bowels when delivered in unfit condition.

The treatment of achylia and subacidity should be based on the following principles. The secretory activity of the stomach should be taxed as little as possible, and when still present should be stimulated. Sparing and stimulation are the object of dieting and medication, both of which further intend to overcome whatever effects follow the gastric secretory depression.

Dietetic Treatment

A diet arranged with a view of sparing secretory activity calls in the first place for a thorough mechanical preparation of all articles of food. When discussing the same indications in the chapter on Irritative Secretory Disorders we stated that the stomach is given the task of dividing up food by dissolving all enveloping substances, such as the fibrous tissue of meat, the gluten of bread, and the pectin and other layers of raw vegetables. When gastric juice is missing this task cannot be accomplished, and it is therefore essential in the first place to eliminate from different foods all these substances, which are only dissolved and digested by the activity of the gastric secretion, and which, when they enter the intestines unchanged, are not affected by the pancreatic and intestinal secretions, but pass undigested with the feces. These undigested tissues are frequently the cause of intestinal trouble by undergoing putrefaction; they further prevent the intestinal secretions from reaching the enveloped elements (meat fiber, starch globules, etc.). Where the latter remain undigested they are another source for intestinal putrefaction and fermentation. Food should therefore not only be freely divided, but also properly prepared by cooking, which partly dissolves these enveloping

tissues, as Backel has demonstrated for vegetables, A. Schmidt for meat, etc.

Meats.—This consideration shows that the popular advice of offering patients with low gastric secretion raw scraped beef has no justification. Scraped raw beef should be entirely eliminated from dietary of such patients, further, for the same reason, raw ham and other raw uncooked meats, sausages, etc. All meats should be given well done and after their fibrous tissues have been removed as much as possible. In aggravated cases they should be hashed and puréed. In milder cases, when allowed in natural form, preference should be given to those types which have tender meat fibers and little fibrous tissue, such as lamb, lean fish (cod, halibut, haddock, striped bass, red snapper, smelt, perch, etc.), lean poultry (chicken, turkey, capon, the white meat preferably), while all fat meats (pork) and those with a coarser fiber (roast beef, duck, goose, and other fowl), oily forms of fish (salmon, mackerel, eel, bluefish, pompano, shad, etc.), should be altogether prohibited. For further details in regard to lean and fat types see the corresponding list in diet for Hyperacidity.

The above albuminous foods, however, are permitted only with normal activity of the bowels. When intestinal putrefaction prevails all these articles of food should be eliminated, even when not causing gastric discomfort, because they are particularly prone to intestinal putrefaction.

Eggs.—Eggs, ordinarily permitted, should also be forbidden when intestinal compensation is disturbed. When poorly digested, egg-albumin very readily undergoes putrefaction in the bowels, particularly raw egg-albumin, which, if not dissolved by gastric secretion, is just as little digested by trypsin as raw fibrous tissue.

Milk.—The tolerance of milk also depends to a great extent on the condition of the bowels. With normal activity of the bowels milk is usually an excellent food in these conditions, and should be given in the form which best agrees with the patient. The digestion of plain milk is aided by adding some salt. Fermented milks, koumiss, matzoon, sour milk, buttermilk, etc., are often beneficial in cases with constipation. When intestinal disturbances are present milk should be given tentatively. In certain cases milk proves a good intestinal antiseptic and the patient is cured of his intestinal putrefaction and diarrhea when put on an exclusive milk diet. Not infrequently, however, milk increases the intestinal disorder in cases where all albuminous substances fall a prey to putrefaction.

Starch.—In such cases all albuminous foods (meats, eggs, milk, etc.) should be entirely eliminated for a while and the patient put on an exclusive diet of carbohydrates, particularly starches.

In any event, even when albuminous foods are tolerated, starchy foods should form the staple diet in these cases for the good reason that the conditions for the digestion of starches are particularly favorable here, and for the further reason that the predominance of carbohydrates in the diet-

ary is the best counterbalance to the tendency of these patients to develop intestinal putrefaction of albuminous matter. Even with the so-called starchy foods, however, we must be aware of the necessity for removing enveloping substances, which, as a rule, are of an albuminous character. Bread, for instance, is not a good food on account of the gluten which, like all enveloping tissues of albuminous character, interferes with the action of saliva and intestinal secretions. Starchy foods are therefore best given in the form of gruels, of thoroughly boiled cereals, as soups made of fine flours, as purées of potatoes and other vegetables. Very valuable in particular are soups or purées made of leguminous flours, on account of their high nutritive value.

Butter.—Butter is very useful here and should be given liberally as long as the motor activity is normal and neither gastric nor intestinal fermentation forbids its administration. It is always preferable to add it raw to the different foods.

Preparation of Foods.—This very important indication of having all foods as far as possible mechanically finely divided need not interfere with the palatability of the food. Yet special care should be taken to prepare these and other foods in a palatable manner and to serve them in a way enticing to the appetite of the patient, which, as Pawlow has taught us, is a strong provoker of gastric secretion.

General Rules.—While it is necessary to rule out all complicated dishes and heavy sauces in the preparation of plain courses, such articles of food should be employed as are known to stimulate gastric secretion. In the first place, the extractive substances of vegetables as well as of meats, which are either used in preparing soups, purées, etc., or taken pure in the form of broths of different kinds, should be employed. Another valuable ingredient is table salt, which may be added to almost any kind of food. It acts beneficially, however, only in small quantities, and in the concentration of a normal saline solution. Other constituents should be used very sparingly. Von Korcynski demonstrated that most condiments, instead of stimulating secretion, irritate the mucosa and produce a transudation of alkaline fluid which dilutes whatever digestive secretion is present.

Stimulation of gastric secretion is also pleasantly accomplished by alcoholic drinks of different kinds, which often aid digestion directly and indirectly by stimulating the appetite, provided they are taken in moderate quantity and in diluted form. When chronic gastritis is the cause of diminished secretion all alcoholic drinks should be avoided. Mildly carbonated waters often act as a stimulant. Of other beverages weak tea, cocoa, and coffee are allowed when tolerated.

In arranging a diet for patients of this type we should be aware of the necessity for stimulating digestive activity. While adhering to the general rules laid down here we must provide for a frequent change of dietary.

In a case with pronounced disturbances it may be indicated to restrict the patient for a period of time to only one kind of food, gradually adding one or another in order to find out what really agrees with him. It may further be advisable to restrict each individual meal to one or only a few different kinds of food. Aside from this, however, we should try to make the diet list as liberal as possible, in order to allow a frequent change. Copious meals should be avoided; it is preferable to give a greater number of small meals.

Medical Treatment

Hydrochloric Acid.—Among all medical means hydrochloric acid ranks foremost and is really *the* drug in the treatment of all depressive secretory disorders. It should be administered regularly, liberally, and over long periods of time. To secure its effectiveness, however, larger doses should be given than are ordinarily prescribed, about 20 drops of the diluted hydrochloric acid with each meal, three to five times a day, bringing the total daily amount up to about 100 drops. In order to avoid irritation of the mucosa it must be well diluted, the 20 drops in 250 to 300 c.c. of water, to be taken through a glass tube partly before, partly during, and partly after meals. While even these doses are very small when compared with the amount secreted under normal conditions, and while the acid is not so thoroughly mixed with the chyme as the natural secretion, nevertheless modern investigations by Leo, Bickel, Tabora, and others have clearly demonstrated that hydrochloric acid is useful and effective in many different ways. Regarding the use of HCl see reviser's criticism.

1. It is an excellent appetizer, in many cases surpassing in effectiveness bitters and similar drugs.

2. Although the quantities taken are too small to replace the missing natural secretion they nevertheless directly aid gastric digestion by dissolving to a certain degree the enveloping tissues, particularly gluten, and less efficiently fibrous tissue. This is partly brought about by the activating effect of hydrochloric acid on gastric ferments, which are rarely completely absent even in cases of achylia gastrica.

3. It displays its antiseptic influence on gastric and intestinal contents.

4. It regulates the pyloric activity, preventing too rapid evacuation of the stomach and overloading of the bowels with undigested food.

5. Not less and probably more important than the direct results of hydrochloric acid medication on gastric digestion are its indirect effects. It has been shown that, where glandular activity is still present, hydrochloric acid taken by mouth greatly stimulates the gastric glands in answer to the ingestion of food with a more profuse secretion. Medicinal doses further stimulate the secretion of the pancreas, which means not only improved intestinal digestion, but also diminished intestinal putrefaction.

The result of scientific and experimental work fully substantiates the time-honored custom of administering HCl in all cases of diminished or missing gastric secretion.

Ferments.—The result of investigation in regard to the administration of ferments which have been and still are extensively used in these conditions is much less favorable. Aside from the fact that most of the preparations in the market quickly lose their effectiveness, it has as yet not been demonstrated that when given in an effective state they really aid the digestion in the stomach. This applies equally to the different preparations of pepsin, pancreatin, pancreon, and papain, all of which have been recommended for this purpose. We have already mentioned that the gastric enzymes are rarely totally absent, so that the administration of HCl is much more important than that of pepsin and other ferments. Still, while a scientific explanation is yet wanting, we must admit the empirical fact that the addition of pepsin (or some other ferment) increases the effectiveness of the hydrochloric acid mixture, not in all, but in certain cases. However, it is necessary to add the ferment in its original form as a powder to the HCl mixture, about 10 to 15 gr. (0.75 to 1.0 gm.) being given as the dose.

The suggestion of French authors to give the natural gastric secretion of dogs (gasterin—Mathieu and Laboulais), or of pigs (dyspeptin—Hepp) has found little favor, principally because the efficiency of these preparations could not be corroborated by other investigators (Erb, Fleiner, etc.); so that there seems little justification for prescribing these very expensive remedies instead of the effective and inexpensive HCl.

Bitters.—Science says little in favor of bitters, which from time immemorial have been given with the intention of stimulating gastric secretion. The literature on the action of bitters is full of contradictions, probably because most investigators have examined their effects in animals.

Reichmann, who studied their effect in human digestion, states that bitters act directly on the glandular apparatus and when given from half an hour to one hour before meals greatly increase gastric secretion. Pawlow and his pupils give a different explanation and attribute to the bitters a very important action. Considering appetite the most powerful instigator of gastric secretion they claim that the bitters cause a reflex secretion by their effect on the sense of taste. According to Pawlow's ideas the bitter taste provokes pleasant impressions of food by contrast and thereby increases the appetite which, in turn, acts as a stimulant of gastric secretion.

To get the full benefit of this reflex action bitters should be given shortly before meals, which corresponds with the popular custom when administered with the intention of increasing the appetite. The effect would then not be due to any real action of the drug, but in part to

suggestion produced by the impression which the bitter taste makes upon the patient. However this may be, the consensus of opinion among physicians is that the administration of bitters is usually followed by a distinct improvement in gastric digestion and often by an increase in weight, which fully justifies their liberal employment. Since their effect in all probability must be attributed to the one property common to all these drugs, their bitter taste, it is merely a matter of personal preference which one is selected. The following are used: quassia, calumba, condurango, hops, and others administered in the form of infusions, tinctures or extracts of different composition.

As effective stimulators of appetite and gastric secretion we further mention the different tinctures of cinchona bark and tincture of nux vomica, which may be given alone (from 10 to 15 drops per dose) or in connection with the bitters.

Carbolic Acid, Creosote, and Other Aromatic Substances.—Very useful in these conditions are carbolic acid, creosote, and other aromatic substances obtained from wood tar. When given in small quantities they stimulate appetite and gastric digestion, which is probably aided by the antiseptic action of these drugs as they prove particularly valuable when motor disorders are associated with a depressive state of secretion. Carbolic acid is best administered in silver-coated pills in doses of 0.03 to 0.05 gm. (½ to ¾ gr.), creosote in similar doses in connection with oil (cod-liver oil) in capsules, or in fluid form in connection with the tincture of gentian [creosote, 1.0 gm. (15 gr.); tincture of gentian, 5.0 gm. (75 gr.), 5 to 15 drops, well diluted in sugar water or sherry, and administered before meals].

Orexin Hydrochlorate.—Orexin hydrochlorate was recommended by Penzoldt in doses of 0.3 gm. (5 gr.) in powder or tablets as a very powerful stimulator of appetite and gastric secretion. Opinions as to its value vary greatly. It often irritates the stomach and is poorly tolerated.

Sodium Chlorid Waters.—We have already mentioned the stimulating effect which weak salt solutions have on gastric secretion. They may be advantageously employed in the form of natural sodium chlorid waters, which usually contain CO_2, another stimulator of gastric secretion. Waters belonging to this class are those of Saratoga in this country, Bourbonne in France, and Wiesbaden, Kissingen, and Homburg in Germany. It is true that many patients get better results from a treatment at a spa because they are free from work and care and submit more readily to the strict régime which goes with the treatment, but, as a rule, there is no necessity in cases of plain subacidity for the patient to undergo the exertion and expense of a long journey. The waters can be taken systematically at home, using either the imported natural waters or waters prepared by dissolving the salts gained from the different springs.

They display their stimulating action best in cases of subacidity connected with chronic gastritis and we shall discuss this special indication in the section on Chronic Gastritis. Even with plain functional subacidity they often prove beneficial, while little result can be expected from their employment in cases of complete achylia gastrica. The waters should be administered warm. In every case, whether taken at the spa or at home, great care should be taken to give only small or moderate quantities, about 4 to 7 ounces before breakfast, and from 3 to 5 ounces before the other meals, leaving thirty to forty-five-minute intervals.

In cases where the secretory depression is associated with muscular atony and motor insufficiency, only small doses should be allowed, and these only when they act beneficially; otherwise all these waters should be prohibited. Where myasthenia is present the taking of large quantities of any of these waters may have a very deleterious effect.

Gastric Lavage.—Gastric lavage is a decidedly more powerful means of stimulating gastric secretion than internal lavage by the drinking of these waters. We shall see later on that the stimulating effect of lavage is displayed to best advantage in all cases of chronic gastritis, with and without impaired motility. Yet it should be clearly stated that even in cases of pure functional subacidity lavage, when properly administered, often proves the most efficient method of stimulating the inactive glandular apparatus. This effect is due partly to the improved state of the circulation which follows repeated moderate distention and contraction of the stomach, and partly to the direct chemical influence of the fluid used for lavage. The great advantage of lavage is that the fluid, after acting, can be removed from the stomach. Even so not more than 300 c.c. should be poured into the stomach at a time, and this should be completely siphoned off in order to avoid overdistention.

Solutions may be administered by the so-called stomach douche, as first recommended by Kussmaul-Malbranc, instead of by ordinary lavage. In using a special douching tube, as devised by Rosenheim and others, the irrigation under high pressure increases the stimulating effect by striking the walls of the stomach in many fine currents with considerable impetus.

We use for stimulating purposes solutions of sodium chlorid (1 teaspoonful to 1 quart of water), or solutions of bitter tonics. Kussmaul described the benefit of solutions of hops and quassia in his first article on gastric lavage, and Fleiner thirty years later confirms the observations of Kussmaul made on an unusually large clinical material. Although not conforming with Pawlow's ideas, who believes that the bitters act only through their bitter taste, the application by lavage of solutions of bitters often has an unmistakable effect in improving appetite and gastric digestion. This clinical observation was corroborated by Hemmeter, who tried infusions of gentian and cinchona, and by others who employed these and

other bitters (fluid extract of condurango 5.0:1,000.0 water). With us the application by lavage of solutions of bitters is one of the routine methods of treatment.

Gavage.—We wish to mention here another method of treatment which we learned in Kussmaul's Clinic, and which we have employed ever since in suitable cases, often with striking benefit. In cases where depressive secretory disorders are the result of anemia and general asthenia, following acute or chronic infectious diseases and general nervous breakdowns, a vicious circle is created inasmuch as the diminished secretory activity interferes with digestion and consequently with nutrition. It is particularly the lack of appetite, and not seldom an aversion to all kinds of food, which makes it so difficult for patients of this type to take and digest an amount of food sufficiently large to raise the state of their nutrition. In such cases, and after gastric lavage, a meal consisting of a thick gruel or a soup of high nutritive value should be poured into the stomach before the tube is withdrawn. The stimulation of gastric secretion and of gastric activity as a whole, occasioned by lavage, puts the stomach in good condition for the digestive act, which sets in immediately and without the need of swallowing food on the part of the patient. Once this food is taken care of, it serves the system well not only by improving the state of nutrition in general but by raising the secretory activity of the stomach in particular. It is often remarkable how quickly in such cases the appetite returns for the other meals of the day, after lavage and forced feeding in the morning set the digestive activity a-going. The French have recommended and extensively used this method (gavage) in tuberculous patients, when the attempt to increase the state of nutrition meets with difficulties on account of depressive secretory disorders and lack of appetite.

MOTOR DISORDERS OF THE STOMACH

Motor disorders are frequently symptoms of other diseases of the stomach (hypersecretion, gastritis, ulcer, cancer, etc.), and should then be treated in connection with the disease with which they are found associated. Motor disorders of this type have been classified as secondary when compared with another group in which they form the main disturbance and appear to be of independent character. Upon closer examination, however, it will be seen that even these so-called primary motor disorders are almost invariably symptoms of other conditions, of systemic diseases, of diseases of the blood and of the nervous system; so that it is always essential to clear up the underlying cause if treatment is to be successful.

The attempt to classify more completely the different types of motor disorders has created a good deal of confusion, inasmuch as one author

bases his differentiation upon disturbances of function (for instance, lack of tone and diminished peristalsis—atony), another upon the result of the disturbed function (delayed evacuation—motor insufficiency of first degree; stagnation—motor insufficiency of second degree), while a third classification describes anatomical conditions (dilatation of the stomach, etc.)

Although it is of great importance for the understanding and for the treatment of the individual case to analyze the different features of the disturbance, for our purposes of description it is more practical to adhere to the old classification of "Atony" and "Dilatation." Both terms represent well-defined clinical pictures, observed in distinct groups of patients, and, while named according to the rule, *a potiori fit denominatio,* each picture in a different degree presents on closer inspection, combined or successively, the different features of disturbed motor function, its effect on evacuation, and eventually anatomical changes, all intimately related.

Motor Disturbances.—Motor disturbances include diseases both (A) with and (B) without motor insufficiency.

A. Motor disturbances with motor insufficiency are grouped with diseases of:

a. Organic origin.
b. Functional origin.
c. Temporary nature.

a. Organic motor insufficiency can be caused by:

(1) Organic obstacles in or around the pylorus or duodenum (cancer, ulcer, scar-tissue, benign tumor, extrinsic adhesions, constrictions, etc.). This form is the most important and the most frequently encountered in practice.

(2) Organic diseases of the stomach located elsewhere than at the pylorus (cancer, ulcer, inflammation, chronic gastritis).

b. Functional Origin.—Motor insufficiency with functional origin develops:

(1) After atony or ptosis, especially in enfeebled, anemic or otherwise debilitated individuals.

(2) Acute dilatation of the stomach, contrary to the chronic form, belongs to this group.

c. Temporary motor insufficiency may develop in an otherwise normal stomach during an attack of acute indigestion (so-called "spoiled stomach"), migraine, or of cholelithiasis, gastric crisis, pylorospasm, intermittent gastrosuccorrhea, etc.

The organic and chronic forms of motor insufficiency are dealt with in the subdivision of Complications of Gastric Ulcer. Acute dilatation of the stomach is discussed in this chapter.

B. Motor disturbance of a functional character without motor insufficiency.

a. Peristaltic insufficiency or atony.
b. Descensus of the viscus or gastroptosis.
c. Different motor alterations of a psychic or nervous character.

While atony and gastroptosis are properly conditions rather than diseases, and are manifestations of asthenia universalis congenita, the members of Group *c* are mostly symptoms of neurasthenia or hysteria, or accompanying signs of a constitutional deficiency manifested as a functional disease; their presence is only temporary and they have been dealt with in the section on Gastric Neuroses.

To Group *c* belong:

Gastrospasm, cardiospasm, pylorospasm.
Peristaltic unrest (Kussmaul).
Neurotic hypermotility.
Nervous vomiting.
Regurgitation.
Eructation, aërophagy.
Pyrosis.
Rumination or merycism.
Singultus gastricus nervosus (hiccup).
Pneumatosis and asthma dyspepticum.
Pyloric incontinence.

Gastric Atony

(*Myasthenia Gastrica*)

Fenwick characterizes gastric atony as "a diminution of the elasticity and strength of the muscular coat of the stomach, whereby the organ is rendered unduly distensible and is prevented from emptying itself within the normal period of time."

Lack of tonicity may cause a great deal of discomfort and is the most frequent disturbance encountered in cases of so-called nervous dyspepsia. The effect of diminished peristalsis on the evacuation of the viscus varies greatly in different patients and with the individual patient at different periods. Some patients experience periodically a state of more pronounced motor insufficiency, either caused by undue overloading of the stomach or as an effect of constitutional derangements (for instance, in migraine). During such periods it may happen that the stomach does not empty itself over night, while ordinarily "stagnation" does not occur in gastric atony.

Gastric atony, when not associated with other gastric diseases (gastritis, ulcer, etc.), is not a strictly local disease of the stomach. It is

either caused by anemia and subnutrition, particularly when connected with acute and chronic infectious diseases (tuberculosis, syphilis, etc.) or intoxication, or it is the effect of derangements in the nervous system (neurasthenia). In the vast majority of cases in which gastric atony is the predominant disturbance it is the symptom of a condition which Stiller first described as "congenital general asthenia," usually observed in patients showing the habitus enteropticus, the constitutional inferiority finding expression in symptoms of motor disturbance such as peristaltic insufficiency. Atony is simply a symptom, which may be demonstrated by X-ray, or observed at the bedside. Besides the splashing sound, abnormalities of the gas bubble—first physically demonstrated by A. Koranyi—are able to supply us with significant data. Atony is usually associated with other signs of functional disorders or sensory manifestations, which are often wrongly attributed to the atonic condition. To be sure some of them may be present as sequelæ of the delayed clearance which may accompany the atony, or there may be discomfort due to the overloading and consequent overdistention of the atonic muscular wall, but the functional and sensory disturbances may also be present without these conditions.

Kussmaul was the first to discriminate between atony and dilatation, and emphasis should always be placed upon this distinction. Boas's term, "muscular insufficiency of the first degree," which he identifies with atony, is inexact, for, according to our observations—which are in full agreement with those of Bettmann and others—muscular insufficiency is not implied in the term "atony." In order to recognize more minute alterations or impairment of the stomach's motor power, Galambos advised the withdrawal of the ingesta after the test meal (Ewald's test breakfast) combined with Mathieu Raymond's method of estimating the total quantity after ninety minutes, instead of waiting only forty-five or sixty minutes. If hypermotility exists, the stomach will be empty after this lapse of time, but if normal motility is present small total quantities (about 50 c.c.) will be observed. Subjects with delayed evacuation will show higher quantities according to the degree of motor impairment present. If the examination is made after the lapse of only forty-five minutes the difference between the figures for the total quantities in the normal motility cases, and those showing hypermotility, will not be so pronounced as they will be if examination is performed after ninety minutes.

The knowledge of the nature of the underlying cause is of paramount importance for a proper treatment. We shall discuss here in the main the last-named form, which is caused by a derangement in the nervous system. The general principles of treatment are the same for other forms which, in addition, require treatment of the concomitant chlorosis, tuberculosis, etc.

When a tendency to gastric atony is inherited, its treatment should begin during infancy. Children of this type should be educated with a

view of developing the physical rather than the mental activity of the system.

During the later periods of life these patients are often greatly handicapped by frequent attacks of dyspepsia and consequent malnutrition, unless they make up their minds to live strictly within the limits of their inherited means. They must be taught to realize that the disposition to weakness and relaxation of the muscular system in general, and of the stomach in particular, is with them a constitutional shortcoming, which they have to reckon with in arranging their mode of life and diet. They must avoid overtaxing the system by physical and mental strain, undue excitement or worry, overindulgence in sexual affairs, in eating, drinking, smoking, etc. Not only the patient, but the physician as well, should bear in mind the constitutional limitations of his patient when advising treatment for him. These patients are usually undernourished, and on consulting physicians are generally urged first of all to increase their weight by liberal eating. While it is undoubtedly an important part of the treatment to raise the state of nutrition, yet this should not be done at the cost of aggravating the motor disturbance of the stomach. Especially when a "rest cure" is prescribed for these patients, which in itself may be needed and advisable, the mistake is often made of ordering large quantities of food, and particularly of milk. The large and frequent meals prescribed in the routine scheme of a rest cure tend to exhaust the muscular power of the stomach, and it thus frequently happens that these patients date the beginning of their gastric suffering from the time when they underwent a rest cure. Similarly we find that patients refer the onset of gastric ailments to the time when they were convalescent from an operation or from an acute infectious disease and had an atonic stomach overloaded by large quantities of fluid and semifluid foods.

Diet.—In arranging a diet in gastric atony we have to meet two indications: (1) to provide nutritive material in sufficient quantity to improve the general nutrition; and (2) to give it in such a form that it will tax the muscular activity of the stomach as little as possible. A diet consisting principally of nutritive fluids, such as milk, thick soups, etc., has been recommended as particularly suitable on account of the observation that fluids leave the stomach quicker than solids. In selected cases such a diet is well tolerated and helpful if not continued for too long a period of time. As a rule, however, the quantities required for improving nutrition in these cases are so large that they are apt to overdistend the stomach and thereby still further weaken the enfeebled walls of the viscus instead of raising their tonicity. In order to avoid overdistention another device proposes to exclude fluids altogether, putting the patient on a so-called "dry diet." This form of diet is especially recommended for patients who have to go about working; for patients who can afford to rest there is less danger from overdistention by fluids when in a recumbent position. Occasionally

we have had good results from putting suitable cases on a dry diet for a limited period of time. As a general principle, however, it is not advisable to enforce a dry diet for long periods of time. Moritz has shown that all solid food has to be liquefied by the secretions of the stomach, so that no great gain is derived from a dry diet which, on the contrary, may make great demands on the activity of the stomach in calling for the secretion of the necessary fluid.

In the majority of cases it is therefore better to avoid both schemes, a diet consisting only of fluids as well as a dry diet.

We would say, however, that it is often a good plan to have the individual meal consist either only of fluids or dry food.

In regard to *fluids* we would stipulate the following rules: Milk and thick soups of high nutritive value may be tried and, when tolerated, allowed in moderate quantities, not exceeding 6 ounces at a time. They should not be given with other (solid) food, but as a meal by themselves. Fluids without nutritive value should be avoided as far as possible, although in milder cases small quantities of weak tea or cocoa for breakfast often act as a stimulant. Water is either omitted altogether for a certain period or given in moderate quantities between meals, but under no condition with meals. Particularly harmful are waters charged with CO_2 which, when freed, greatly distend the enfeebled wall of the stomach. For the same reason are forbidden all fermentable drinks (beer, lemonade, etc.).

All *solid* food should be thoroughly prepared, mechanically finely divided, and, if possible, puréed so that it may leave the stomach in quick order. In selecting and preparing different types of food due consideration should be given to concomitant secretory disorders of the stomach, according to the rules given for irritative and depressive secretory disorders.

Preference should always be given to those articles of food which have comparatively high nutritive value in a small volume. When permitted, well-selected lean animal food (meat, fish, poultry, eggs) properly prepared is the most suitable food in this respect. When vegetables are indicated those which are voluminous without being nutritive should be avoided altogether (cabbage, tomatoes, salads, etc.). Starchy vegetables and cereals are especially well tolerated in cases of subacidity. Butter, cream, and oil add greatly to the nutritive value of the meal when not contra-indicated on account of acid fermentation. They further prove valuable in cases with sluggish activity of the bowels. When constipation is present we should further add purées of stewed fruits, honey, milk-sugar, and malt extract. Whatever food is permitted should be taken in moderate quantities; the rule should further be observed not to give too many different courses at an individual meal.

Some of these patients feel more comfortable when taking three prin-

cipal meals of about equal size, giving the stomach between the meals the necessary periods of rest. In other cases it is preferable to give meals consisting of moderate quantities at shorter intervals. The atonic stomach disposes of its contents in shorter time when the patient rests after meals, preferably in the recumbent position.

Medicinal Treatment.—Medicinal treatment plays an inferior rôle in gastric atony. Drugs are recommended for various purposes. It should be stated, however, that good judgment must be exercised lest they do more harm than good. The secretory activity of the stomach deserves full consideration; when hyperacidity is noted we prescribe alkalis, in cases of subacidity hydrochloric acid. Adequate treatment of secretory disorders always benefits the motor activity.

A good deal of restraint should be exercised when atony is associated with gastritis, inasmuch as most drugs are apt to act deleteriously on the gastric mucosa, and thus indirectly aggravate the atony of the muscular coat. Dietetic treatment and lavage prove a much better stimulant in such cases than drugs. This applies particularly to most of the so-called antiseptic and antifermentative remedies which produce very small results unless the motor disorder is effectively combated by the methods of treatment and a quicker evacuation of the stomach accomplished. Prevention of stagnation is the most reliable antiseptic. Of drugs usually recommended as *antiseptics* we mention: salicylic acid 0.32 to 0.65 gm. (5 to 10 gr.), salol 0.32 to 0.65 gm. (5 to 10 gr.), resorcin 0.32 to 0.65 gm. (5 to 10 gr.), creosote, carbolic acid pills 0.03 to 0.065 gm. (½ to 1 gr.).

For *flatulency* peppermint, aromatic spirits of ammonia, ol. cajuputi, charcoal mixtures, validol (5 to 10 drops), etc., are much in use.

As a direct stimulant of the muscular coat we employ *strychnin* or *nux vomica,* either alone or combined with bitters (gentian, columba, etc.). Although some authors maintain that strychnin merely improves the appetite, and that its direct effect upon the musculature is nil, yet it seems to be the general consensus of opinion among practitioners that it has a decidedly beneficial effect in gastric atony. Bastedo regards strychnin and nux vomica as true physiologic tonics having an action on Auerbach's plexus, increasing gastric tone, improving the peristaltic response to food, promoting secretion, increasing sensitiveness, etc. Other drugs advised as directly stimulating the musculature (*ergot, hydrastis*) are not recommendable on account of their harmful action on the gastric mucosa.

Gastric Lavage.—By far the most powerful and the most reliable stimulant of motor activity is gastric lavage, particularly in the form of the stomach douche. Its application is absolutely necessary whenever, during the course of these cases, stagnation occurs and food remnants are found in the fasting stomach. Even in cases without stagnation lavage always proves beneficial when properly applied. When giving lavage by

the stomach douche under high pressure, somewhat cooler water may be employed. Alkaline or sodium chlorid solutions are used according to the state of secretion, antiseptic solutions in case of fermentation, and infusions of bitters when we intend to stimulate secretion.

Evacuation of the Bowels.—As in most cases of gastric disorder regular evacuation of the bowels is of great importance. We must, however, warn against the employment of concentrated saline cathartics and of drastic purgatives, which almost invariably do more harm than good in gastric atony. We should always select the mildest remedies, which are usually the most effective. While methodical drinking cures of natural mineral waters are not indicated, yet the taking in the morning of a small glass of Vichy, Kissingen, or some other appropriate natural water is frequently effective in promoting evacuation. Or we advise cleansing enemas, or small doses of cascara, rhubarb, sulphur, and similar drugs. Only the smallest dose which is effective should be given.

Mechanical Treatment.—As a rule the activity of the bowels is simultaneously benefited by a number of mechanical methods of treatment which are employed in these cases with the intention of improving the muscular activity of the stomach. We refer to different outdoor and indoor forms of exercise and gymnastics, hydrotherapeutic measures of general and local character (hot and cold compresses, Priessnitz bandages, abdominal douches, etc.), to general and abdominal massage, to vibration, and to different electrical treatments. The main effect of all these measures is this, that they promote the abdominal circulation, thereby indirectly improving the muscular activity of the stomach and intestines. It is claimed that massage directly stimulates the muscular coat. Whether faradization exercises any direct influence upon the muscular coat is more than doubtful, whether given intragastrically or percutaneously. Personally we have always preferred the percutaneous application of the faradic and of combined faradic and galvanic (sinusoidal) currents, since it permits of administrating stronger currents and this, at all events, produces a decided improvement of abdominal circulation. When judiciously employed any of these methods may improve gastric atony. However, we wish to point out here once more the absolute necessity of properly considering the constitutional element which is the predominant factor in these cases. In prescribing and administering mechanical methods of treatment we must always bear in mind the constitutional limitations of the patient. A great deal of harm is done by advising the patient in a general way "to take exercise," or by having him undergo vigorous treatment which overtaxes his resources, with the result of still further weakening the muscular activity instead of strengthening it. All these methods of treatment require careful dosage just as much as the administration of drugs. We should particularly avoid employing several of these methods at one time.

Gastroptosis

Gastroptosis, the downward displacement of the viscus, is either inherited or acquired. Although the congenital type of gastroptosis was clearly described by Kussmaul, it is to the credit of Stiller to have first demonstrated that inherited gastroptosis associated with dislocation of other abdominal organs (enteroptosis) is only part of a peculiar constitution which he designated as "asthenia universalis congenita." This constitutional anomaly is met with in the vast majority of cases.

The development of the acquired form is attributed to attenuation and stretching of the abdominal wall after frequent confinements, the removal of ascites, and abdominal tumors; to the flattening of the diaphragm by pneumothorax and pleuritic effusions; to the downward pressure of an enlarged liver and pancreas; and to the debilitating effect of acute and chronic diseases causing emaciation.

Gastroptosis of itself need not give rise to any symptoms whatsoever either in the acquired or in the inherited form. As long as no symptoms are present the displacement itself does not require treatment.

Symptoms appear when the viscus becomes atonic. In both forms there is a pronounced disposition to develop atony. When the latter occurs treatment should be conducted along the lines described in the section on Gastric Atony. Symptoms caused by gastric atony are apt to irritate the nervous system and interfere with the result of the general treatment, especially in cases of the congenital form which show a great tendency to nervous disturbances.

A great deal of confusion still prevails regarding the relation of gastroptosis and disturbances of the nervous system so frequently encountered in these cases. Some firmly believe that neurasthenia develops secondarily to the gastroptosis, a conception especially held by surgeons who proposed operative measures to correct the displacement of the organ (Rovsing, Beyea, and others). This conception is certainly erroneous in so far as it considers the displacement of the organ as the paramount factor. The neurasthenia which almost invariably exists in these cases is constitutional and is part of the general asthenia which Stiller describes as typical for cases showing inherited gastroptosis. Patients who present the habitus enteroptoticus (with gastroptosis) are predisposed to neurasthenic disturbances and to gastric atony. The mere correction of the displacement of the stomach in no way changes this constitutional asthenia, and operations undertaken for such a purpose are therefore unwarranted. Surgical procedures in these cases are liable to do great harm by insults to the nervous system, which it takes the patient a long time to overcome. Operative intervention (gastroduodenostomy) should be reserved only for those rare cases in which there is pyloric stenosis due to kinking (Rov-

sing). Another operation, which can be performed in extreme cases, is gastropexy, by which Rovsing obtained final cure in about 50 per cent of the operated cases.

On the other hand, a tendency seems prevalent to underestimate the importance of the local gastric disturbance. It is undoubtedly correct to direct the principal attempts of treatment to the organism as a whole, trying to improve the condition of the nervous system by regulating the mode of life and the diet, and by prescribing *sedatives* (bromid, valerian, etc.), and *tonics* (strychnin, arsenic, iron, etc.). Yet we should not forget that the subjective symptoms directly provoked by the effects of gastric atony have a very harmful influence upon the nervous system in such cases and may establish a source of constant irritation which interferes with all attempts at general treatment. The proper consideration and direct treatment of the gastric atony, and of the secretory disorders usually associated with it, are of great value in cases of asthenia universalis congenita with gastroptosis and neurasthenia.

Looking at it from this point of view, we must admit that in these cases the question of operative treatment may turn up when gastric atony has led to the development of atonic dilatation which proves stubborn to all medical methods of treatment and steadily interferes with the proper nutrition of the patient. We discussed this indication in the section on Chronic Atonic Dilatation. It is of comparatively rare occurrence. A stomach which does not constantly show stagnation should never be operated upon for gastroptosis.

Aside from the general treatment of the whole system and the special treatment of gastric atony we have to mention as the only measure directly prescribed for the gastroptosis the application of an abdominal belt. Numerous varieties have been devised for this purpose, but none of them will suit every patient, and it is therefore necessary to have a belt made which will be comfortable to the patient and at the same time answer the purpose of supporting the stomach and holding it in position.

Treatment of Motor Alterations of Neurotic Origin

In dealing with this question it should be borne in mind that motor alterations of neurotic origin are not diseases sui generis. Often they are but symptoms of a general neurasthenia, hysteria, or psycho-asthenia, associated with other functional or sensory disturbances of the stomach. Everything detailed in the section on Gastric Neuroses concerning general treatment may also be applied in the conditions here considered. For local treatment we must undertake to search out and deal with the underlying causes of such phenomena as muscular spasms provoked by hyperacidity, hypersecretion, ulcer, etc., or nervous vomiting in its juvenile, idiopathic, periodic or reflex forms.

J. Friedenwald discriminates between *vagotonic* and *sympathicotonic* symptom complexes, recommending in the first group—which comprises such manifestations as hyperperistalsis, vomitus, etc.—the employment of atropin, belladonna and adrenalin; in the second group—made up of conditions such as atony and pyloric incontinence—medication with pilocarpin and pituitrin. The stimulating effect of the pituitary extract on the pyloric tonus and peristaltic function was demonstrated by Gorke and Deloch. J. Kaufmann uses calcium in autonomic spastic conditions.

In aërophagy and pneumotosis the introduction of the rubber tube offers the best and quickest measure of relief, as it will almost instantly abolish all symptoms of tension. In pyrosis, acid eructation, regurgitation and vomitus—especially when combined with hyperacidity—the administration of alkalis may be useful. Electric intrastomachal treatment, lavage of the stomach, duodenal feeding (Einhorn), or dilatation of the pylorus by means of bougies, etc., may, in rare cases, prove temporarily useful.

Acute Dilatation of the Stomach

Although long known to internists, acute dilatation of the stomach has recently become a topic of great interest, since its frequent occurrence after operations has been noted. Paresis of the stomach, accompanied by excessive secretion of gastric juice, is observed as an effect of the toxic action of the anesthetic after operations of every kind, and may be aggravated by mechanical insults to the upper abdominal cavity during the operation. When this postnarcotic paresis is not carefully watched, errors in diet, particularly early feeding and overloading of the stomach by fluids, may have a marked influence in developing a pronounced and eventually enormous paralyzing dilatation of the stomach, a dangerous and not infrequently fatal condition. In a certain group of these cases gastromesenteric ileus is produced by the pressure of the mesenteric root on the third part of the duodenum. This was first discovered by Kussmaul, who considered this mechanical obstruction as secondary to and caused by the traction of the primarily dilated stomach, which occurs particularly with downward displacement of the overloaded viscus. Peyer, in a recent study of this subject, differentiates between this form of primary paralysis of the stomach and a second form, in which the obstruction by the pressure of the mesenteric root is in evidence before the paralytic dilatation of the stomach has developed. The latter form is clinically characterized by setting in with shock, increased peristalsis, stiffening, and delayed dilatation of the stomach. Whatever the primary factor may be, when once developed acute dilatation presents a vicious circle which must be broken.

The treatment calls in the first place for prompt evacuation of the stomach by means of the stomach tube. This affords immediate relief by

removing often enormous quantities of gastric contents. Lavage should be repeated at short intervals without waiting for vomiting to indicate that the stomach is full again.

The excessive secretion usually continues, and with the paralyzed condition of the stomach it is quite common for no vomiting to occur in these cases. So, from the beginning, we should not wait for this symptom as an indication to evacuate the organ.

To avoid frequently repeated introduction of the stomach tube Westermann secured *permanent gastric siphonage* by passing a tube through the nose into the pharynx and down into the stomach, where it was left in situ for several days. Other surgeons have employed this method of permanent drainage with equally good results and have pointed out as particularly in its favor that it permits the patient to drink unlimited quantities of fluid, thereby adding to his comfort, even when employed in hopeless cases. Without permanent drainage fluids and nourishment by mouth should be omitted, but they should be given by rectum or hypodermically.

Of great assistance is the proper position of the patient. Peyer considers it of even greater importance than the emptying of the stomach. To have the patient lie on his right side is the most effective position, and when this is started at an early date may act prophylactically. The value of this position was first recorded in 1880 by Malbranc, an assistant of Kaussmaul, who recommended it to relieve the compression of the duodenum by the root of the mesentery, which he had observed as causing acute dilatation in cases of chronic dilatation of the stomach. In severe cases the knee-chest position may be tried when the position on the right side is not effective.

Drugs have little influence. Eserin, 0.001 to 0.0015 gm. (1/60 to 1/40 gr.), was recommended, but was found to be without value and usually caused depression. Better results may be expected from adrenalin, particularly in cases in which the symptoms of collapse point to a deficient activity of the chromaffin system. Operative measures are contra-indicated; they can accomplish nothing and are apt to further aggravate the condition.

Besides the postoperative we mention the following types of acute dilatation of the stomach:

1. A type first described by Naunyn occurring in persons apparently perfectly well and which is brought about by the *ingestion* of large quantities of easily fermentable substances. Here the intense fermentation of the stomach contents is the primary factor, and therefore prompt evacuation of the fermenting masses by means of the tube is the most rational and effective treatment. After being cleansed thoroughly by lavage the viscus should be given a chance to contract by prohibiting the

intake of food and fluid by mouth, and by following this later by careful feeding with small quantities of mechanically well-prepared articles of food. This type of acute dilatation is more liable to befall people with an atonic stomach and to supervene in chronic dilatation.

2. Acute dilatation in *infectious diseases* (typhoid, pneumonia, etc.) is one of the manifestations of toxemia. Here, as after operations, acute dilatation is a very serious matter, and the advent of pronounced tympanites should always be a warning against the indiscriminate feeding of such patients with large quantities of fluid. The fluid necessary to flush the system should be given by enteroclysis and hypodermoclysis. In these cases paralysis of the vasomotor nerves, especially in the splanchnic area, is one of the most striking effects of the toxemia, and *adrenalin* may therefore prove of great value in raising the blood-pressure, particularly in the abdominal cavity.

3. We wish to single out a form of acute dilatation which we find rarely mentioned, that is, acute dilatation in cases of sudden severe gastric hemorrhage. Under the heading Gastric Hemorrhage we discussed the use of gastric lavage in such cases and the great benefit derived from its application.

NEUROSIS VENTRICULI OR NERVOUS DYSPEPSIA; ITS RELATION TO FUNCTIONAL DISORDERS

The term "nervous dyspepsia" was first applied by Leube to those stomach diseases occurring without anatomical lesions. Later authors have made various attempts to provide a more exact designation for nervous dyspepsia, which was once considered only a symptom complex, but soon came to be regarded as a disease sui generis. Even to-day we do not possess an exact definition of the disease and each author is at liberty to employ the classification which suits his individuality. While most authors consider all or nearly all the functional disturbances, sensory, secretory and motor in character, as belonging to nervous dyspepsia, there are some who, like A. A. Stevens, maintain that "nervous dyspepsia is applied to a syndrome, made up of various gastric neuroses, in which, however, sensory disturbances are always the most conspicuous."

The aim of diagnosis is to differentiate, by reasoning and exact methods, between diseases which do not belong together. The more exact the methods employed, the further can analysis be carried and the more sharply can differentiation be established. To gather into a group under a common designation a number of pathologic conditions which differential diagnosis separates is a retrogression, and a method without justification. Therefore, those conditions which are now considered as belonging together, and are dealt with under the head of Nervous Dyspepsia, ought

to be separated according to their various manifestations and classified under appropriate designations.

The term "nervous dyspepsia" should, therefore, only be applied to those cases of gastric disorder which (1) present no anatomical lesions in the stomach, nor in any organ correlated with it, and (2) present no functional derangements of the stomach—motor or secretory—either primary or secondary, to some functional or organic disease in some distant organ. In other words the term "nervous dyspepsia" should be reserved for those conditions where the symptoms referable to the stomach cannot be explained except by process of exclusion, which assigns their etiology to some *primary* functional disorder of the *sensory* nerves. As an example of the difficulty of such differentiation we may take bulimia, which may be a genuine gastric neurosis, but is far more likely to be an accompanying symptom in exophthalmic goiter, diabetes mellitus, and similar conditions, and in these latter cases it should not be designated as gastric neurosis.

If the X-ray examination of a case of constitutional gastric disorder shows motor impairment or alterations in tonus, or gastric analysis reveals secretory disturbances, there can be no more question of a genuine neurosis in this particular instance. We are then dealing with a *functional disorder,* which may, of course, be either a sign of stomach disease present at the time as, for example, hyperacidity, or pylorospasm, as symptoms of ulcer, or it can be present provoked reflexly as a secondary symptom of some other disease with its original focus in some other organ, as, for example, the same gastric disturbances in cases of tabes dorsalis, cholecystitis, appendicitis, or disease of the genital tract. When no anatomical lesions can be found in the stomach, nor any disturbance located in a distant organ which can be made responsible for the gastric symptoms, we will then be obliged to fall back on diagnosis per exclusionem: functional disturbance, motor or secretory in character, and only in the absence of even this functional disturbance can the gastric complaints be ascribed to a gastric neurosis.

It is impossible to draw a definite line between nervous dyspepsia and the functional disorders, for we cannot demonstrate any marked difference between two cases in both of which we observe symptoms of sensory disturbance of exactly the same character and degree, the only difference being that in one case we find a higher concentration of hydrochloric acid than we do in the other. Yet such a differentiation, slight as it appears, may be evidence of a fundamental character. As most gastric disorders are functional, establishment of a differential diagnosis in this large domain is necessary, and it becomes all the more important to separate—so far as we may be able to do so—those manifestations which, while presenting many symptoms which would lead us to classify them under a common head, have yet certain points of difference which justify our placing them in a separate category.

Disassociation of Sensory and Functional Disorders.—In functional disorders associated with sensory disturbances the subjective symptoms will either be of the character commonly accompanying such disorders—for example, heart-burn or epigastric pain in hyperchlorhydria—or they may be of unusual character as, for example, the same complaint in achylia gastrica. Lack of relationship between the sensory and secretory symptoms of gastric disturbance was demonstrated by Galambos more than fourteen years ago. According to J. Bauer, the subjective complaints are not due to, nor provoked by peristaltic deficiency (atony), nor by secretory anomalies, but are due to anomalies of the sensory nerve supply, to irritation or impairment of the receptor nerves of the stomach. Dyspepsia in hyperacidity, just as much as in achylia, is not due to secretory or chemical imbalance; it is a neurotic or psychic phenomenon (Struempell, Stiller, Bauer).

Lack of relationship between sensory disturbance and functional disorder (motor and secretory) is emphasized by a consideration of the following facts, which are established beyond question: (1) marked secretory disturbances occasionally exist without any accompanying subjective disorders; (2) grave gastric complaints may be manifest when no anatomical or functional disorders can be discovered; (3) recovery can be observed in cases where functional disturbances persisted. The patients may feel well, presenting no symptoms, the sensory disturbances having been abolished though the functional disorders were still present.

We are therefore justified in assuming that in a given case of hyperacidity the symptoms present may not be due to the excess of acid alone, but are manifestations of concomitant sensory disturbances. Either of these two conditions may be present *without* the association of the other.

Associated and Independent Forms of Functional Disorders and Neuroses.—It can be assumed that an intimate relationship may exist between special centrifugal and centripetal nerve paths, so that irritation of either can be immediately transmitted reflexly to the other, or the stimulus conducted by one set of nerve fibers can—especially in the sympathetic, which lacks the insulating myelinic sheaths—be irradiated directly to other fibers. Where functional and sensory disturbances exist together, we may see that the functional disorders can be both *associated* with the sensory ones, or entirely *independent* of them. Thus, hyperacidity may initiate heart-burn and epigastric pain and, on the other hand, pains may readily produce hyperacidity; but in wholly independent functional disorders a high degree of hyperacidity can exist, either without any sensory disturbances whatsoever, or else in conjunction with symptoms wholly unassociated with the usual manifestations of hyperacidity. If our treatment succeeds in abolishing the existing nerve reflexes we may disassociate the secretory and sensory functions, or the motor and sensory functions, or—in rare cases—all three, and thus effect an apparent cure

of the condition, even if the secretory or motor disturbance still persists.

If we deny the possibility of an interrelation between secretory and sensory disturbance, how can we explain the appearance of certain sensory symptoms in one secretory disorder when they are wholly absent in another? Have we any logical foundation for the assumption of an association between special nerve-fiber groups? Has the assumption any anatomical or experimental basis? According to the experiments of Egan, the ingestion of hot or cold fluid does not affect normal gastric motility, but certain subjects always react to cold fluids by a markedly increased peristalsis, which would seem to indicate a constitutional difference in the motor and sensory innervation of the stomach, the detection of which is only possible with the employment of special means of examination (J. Bauer). Exner and Schwarzmann found that in some subjects the sensory conduction is supplied by the vagus, and in others by the sympathetic, which—according to Bauer—would explain very wide variations in sensibility in apparently normal subjects. There is also the possibility of reflex transmission being easier when the sensory path lies along the vagus than when sensations are carried by the sympathetic and the secretory and motor paths lead through the vagus.

Characteristics.—Patients suffering with nervous dyspepsia usually present other nervous symptoms too, either referable to other organs or of a generalized character. The gastric neurosis may have two forms: that developing in the subject of a general neurasthenia, and signifying merely a localization of a generalized process; and that in which the gastric symptoms form the chief complaint, neurasthenia being only a secondary consideration, the patient sometimes even being wholly unaware of any neural involvement whatsoever. There are also many cases which must be regarded as transitional between these two extremes.

The neurasthenic and hysteric types should not be confused, for we are fully as much justified in differentiating between these forms of gastric disturbance as we are in calling one nervous disorder neurasthenia and the other hysteria, as upon this distinction our prognosis and whole scheme of treatment may depend. While the manifestations of a gastric neurasthenia are persistent, stubborn, and often extremely difficult to combat, those of gastric hysteria partake of the kaleidoscopic character of other hysterical symptoms, appearing and disappearing without apparent cause, constantly changing in character and intensity, and yielding readily to suggestive therapeutic measures.

In designating a gastric neurosis as neurasthenic or hysteric we should not be understood as referring to a special type of disease, for both of these forms are likely to be in evidence in such gastric neuroses as bulimia, hyperesthesia, anorexia, etc. But neurasthenic or hysteric characteristics can be differentiated not only in the restricted forms of sensory neurosis, but also in secretory or motor disorders. For example, heter-

ochylia (Hemmeter) may serve as a prototype of a hysteric secretory stomach neurosis; it is the same condition which Galambos many years ago termed "hysteric stomach neurosis." As more recent textbooks have employed the designation "neurasthenia ventriculi," the necessity of differentiation of the hysteric form certainly seems to be indicated. When we are confronted by a patient who has for years complained of various gastric disturbances, and is completely relieved of all his symptoms simply by the passage of a test meal, we are inclined to accept that this is a case, not of neurasthenic or psycho-asthenic, but of a hysteric type of neurosis.

Forms.—The best known forms of sensory dyspepsia are:

Bulimia, pathological increase of the hunger feeling.

Acoria, loss of the sensation of satiety after big meals.

Parorexia, perversion of appetite.

Anorexia, loss of appetite.

Nervous nausea.

Sitophobia, fear of taking food.

Hyperesthesia of the stomach, increased sensitiveness of its mucous membrane.

Anesthesia of the stomach, as in painless cancer or ulcer. (Gastric hemorrhage and death may occur in patients who never had any pain or stomach trouble, autopsy revealing an ulcer which may have been present for many weeks.)

Gastric idiosyncrasies toward certain articles of food.

Heart-burn, commonly manifested as a burning sensation in the epigastrium.

Gastralgokenosis, gastric pain when the stomach is empty (Boas).

Gastralgia nervosa, psychic pain in the stomach.

Abnormal gas sensations, presenting complaints of too much or too little gas escaping or retained. (In some cases the patient experiences eructions of gas every time his back, neck or extremities are massaged.)

The two new forms, anesthesia and abnormal gas sensation, are established as pure sensory disturbance and assigned to this chapter by Galambos.

Cases presenting visible motor symptoms, such as gastrospasm, cardiospasm and pylorospasm, nervous vomiting, peristaltic unrest, etc., and secretory disorders, such as achylia, hyperacidity, or hypersecretion, cannot be dealt with in this section.

Any one of these forms of nervous dyspepsia may be present as a monosymptom, seemingly an independent disease, or as polysymptom, in the combined form of the sensory disturbances also associated with or accompanying other motor or secretory disorders. All these phenomena can appear in neurasthenic or hysteric guise, and functional disorder of other organs, with general neurasthenic manifestations, may be present.

Some single forms as symptoms can accompany other diseases or conditions which are in no way associated with nervous disorder; for example, anorexia in leukemia, or pernicious anemia; bulimia in diabetes mellitus, or exophthalmic goiter, etc.

Treatment.—A stomach neurosis is a symptom complex signifying the existence of a localized neurasthenia, and all therapeutic procedures must be based upon an understanding of this etiology. Our diagnosis once established, we are confronted with a condition in which no medication nor mechanical procedures of schematic form have any justification whatsoever. In the treatment of nervous (sensory) dyspepsia, and—to a limited degree—in that of motor and secretory functional derangements of the stomach as well, success may be achieved in two different ways: first, by general, and second, by special treatment, adapted to the individual case. The special treatment of each form of disease is the usual therapeutic method as described in the proper section. Here, the general methods should first be briefly discussed.

General Treatment in Sensory and Functional Disorders.—At the outset, let us put the question: Is there any basic principle upon which we can build up a system of therapy applicable to all these cases? All diseases presenting altered gastric function are representative of a very large class, Disqué maintaining that at least three-quarters of all gastric disorders are of a functional, constitutional or nervous character. These functional disorders may each be separately manifested, or they may be combined in a truly protean manner, the combined disturbances including not only the different functions of the stomach, but usually also affecting the functions of distant organs, thereby producing symptoms belonging to the same general constitutional disease. To Stiller must be assigned the credit for discovering that all these symptoms, formerly treated as indicative of different disease entites, are in reality part of the same constitutional disease, which he has called "asthenia universalis congenita." This is a constitutional anomaly, usually presenting a floating tenth rib, now commonly designated as "Stiller's sign." Constitutional secretory insufficiency, constitutional secretory hyperactivity, as also functional weakness of the musculature (atony), etc., are degenerative stigmata, indicative of organic inferiority. When such constitutional inferiority is present it can be associated with sensory manifestations in such a way as to result in the presentation of the most varying complex of symptoms.

If we are successful, if only temporarily, in combating and overcoming the asthenic factor in any given case, it is of small moment whether we are dealing with achylia or hyperacidity. Once the neurotic element is conquered the subjective symptoms will usually disappear even if the functional disorders persist, and in many instances both will soon subside. The first requisite of success is to get the *confidence of the patient.* This is absolutely essential. The mere fact that the patient seeks the physician

because of the recommendation of some other person who has been benefited by that physician's treatment is often of more value than any kind of drug administration, and often the most surprising results may be obtained at the very first consultation. If the first treatment brings no favorable results, the chances of subsequent success are lessened. It is important to elicit a careful history of any previous treatment the patient may have undergone and, if several different methods have already been tried, to find out which one the patient himself regards as of the greatest value. Usually the patient will volunteer this information, frequently requesting that his favorite treatment be continued. If the physician undertakes to prescribe without being fully informed as to all previous therapeutic endeavors, he is quite likely to happen upon some measure which has already been tried in this particular case, and proved wholly useless, and its suggestion would at once cause the patient to lose confidence in his new consultant. A case in point is one where the subjective symptoms were ascribed by the physician to abuse of tobacco, only to be informed by the patient that he never smoked, a mistake which could have been easily avoided by taking more care in the elicitation of the previous history of the case.

A *thorough physical examination* is equally important. We were recently consulted by a woman with a gastric neurosis who complained of such conflicting symptoms as fullness, pressure, dull pains, belching, heartburn, flatulence, and constipation, and was fearful that she was suffering from cancer of the stomach. After a careful examination we assured her that there was absolutely no possibility of the existence of cancer, and within twenty-four hours all her gastric symptoms subsided and an immediate cure took place. The physical examination was the sole therapeutic measure employed. Many times we have seen a test meal, administered only for diagnostic purposes, put an end to all complaints of gastric disturbance. Neurotic individuals not infrequently misunderstand the purpose for which the rubber tube is being introduced, and imagine that it is a heroic therapeutic measure. In one of our achylia gastrica cases with plurisymptomatic gastric complaints for years, the employment of a single Ewald's test meal abolished all the manifestations, and, after the lapse of fifteen years, they have failed to return. While confidence in the physician, thorough examination, or mental suggestion may avail in some cases, in others the careful explanation of the condition and an appeal to the patient's own better judgment will effect a prompt cure of any form of the asthenic manifestations. Methods which bring about the most brilliant results with one patient will wholly fail with another. Where the psychic factor enters in we can make no hard and fast rules by which treatment can be governed. There are cases when the administration of distilled water alone will be more effective in combating hyperacidity than the administration of alkalis.

It is often difficult in a given case to decide whether to employ *general* or *special methods*. General treatment takes the patient's mind off his special condition, while the application of some particular method may serve to concentrate his attention upon it. In cases presenting but a single symptom we are often obliged to resort to local measures but, when we are dealing with a symptom complex, general methods are usually more valuable. It is usually superfluous to try to treat each manifestation separately, for they are all but variant manifestations of the same condition. Suggested measures are hydrotherapeutic procedures, such as tepid baths with gradual cooling of the temperature of the water, cool showers, Swedish douches, cold and warm sponges, rubbings, packs, compresses, Winternitz's cooling apparatus, etc.; electrotherapy is also useful, use of the galvanic and faradic current, high frequency, Franklinization, etc.; massage, Swedish gymnastics, outdoor exercise, or sanitarium treatment, rest cure, isolation from family and excitement, change of scene, and the regulation of professional and personal habits, occupational therapy, prohibition of the use of alcohol and tobacco, restraint upon sexual indulgence; all these measures should be considered as possible therapeutic aids.

Drugs.—Bromids are the most useful drugs. However, many patients will complain that they have already taken bromids for a long time without benefit, and are willing to try anything *but* bromids. In such cases we must do without this form of medication altogether, or we must administer it under some other name so disguised as to escape detection by the patient. Sodium, potassium, ammonium or strontium bromid can best be prescribed in combined form, the effervescent salts often appearing most effectual. For powders we use sabromin. Sedobrol is another good bromid preparation, often preferred by patients. Full doses should be given, if indicated, especially at night, in order to secure proper rest. Useful preparations—if the patient does not refuse them—are ethereal tinctures such as tinct. valeriana etheræ, validol, tinc. moschi moschiferi, tinct. asafœtidæ, Hoffmann's anodyne, liquor ammoniæ anisatæ, aromatic spirits of ammonia, etc. Quinin, phosphorus, strychnin, arsenic, and iron may prove useful in those cases which are complicated with anemia, chlorosis, emaciation, general debility, or in convalescence after an infectious disease. They can be given orally in the form of pills, or, if the patient happens to have confidence in injections, hypodermically, or by the intravenous route. We have not found the effect of intravenous injections very striking, while often good results have followed the use of internal medication, when given in good combination in satisfactory dosage. In advanced age, when arteriosclerosis may be present, iodin and diuretin may be required; while complicated with climacteric, or dysmenorrheic complaints, ovarian extracts seem very effective. Constipation is frequently an attending complication, and should never be left unconsidered.

A good cathartic is often an excellent stomachic as well. Mild saline preparations such as Carlsbad salts, phenolphthalein, sal Seignette (Rochelle salts), also rhubarb, senna, etc., are effective. They may be given alternately with olive oil used as an enema, and with glycerin suppositories, etc. In some cases the treatment may be combined with a fattening or reducing cure that is designed to reduce obesity, or to increase weight.

But even though the advantages of general treatment have been stressed, there are, of course, cases where it appears expedient to employ special local treatment as well. This may be either instrumental or accomplished by the use of drugs.

Local Treatment.—Electricity may be applied to the stomach through the abdominal wall, or—in unusually stubborn cases—intrastomachally; also cold compresses, hot flaxseed fomentations, the Winternitz cooling apparatus, massage, etc. Lavage may also be useful in some patients.

The most commonly used drugs are bitter tinctures which serve to increase the appetite (experimentally proved by Straschesko), like tinct. chinæ compositæ, tinct. amaræ, tinct. gentianæ, tinct. nucis vomicæ, etc. Bitter teas can serve the same purpose: herb. galeopsidis grandifolii, herb. lichen island, herb. trifolii fibrini, marubii albi, etc.

Besides these, in cases of gastralgia, morphin, atropin, belladonna, eumydrin, opium, pantopon, papaverin, heroin, dionin, codein, chloral hydrate, bromural, adalin, medinal, aspirin, pyramidon, phenacetin, etc., may be given, singly or combined, in hypodermic injections, orally, or in suppositories.

In cases of hyperesthesia, we may use alkalis such as sodium hydrocarbonate, citrate or phosphate, magnesia usta or peroxid, bismuth subnitrate or carbonate, anesthesin, aqua chloroformi, Hoffmann's anodyne, cognac or whisky, argentum nitricum (Rosenheim), especially in cases of amyxorrhea (J. Kaufmann), food rich in protein, such as milk and eggs, should be administered.

When we are dealing with anorexia, useful medicaments will be orexinum tannicum and condurango—in decoction or in wine—or decoct. chinæ chalisaiæ and sometimes acid. sulphuricum or hydrochloricum dilutum, pepsinum, etc.

SECONDARY STOMACH DISEASES

Gastric disorders secondary to organic diseases elsewhere in the body should not be classed as diseases sui generis, and are usually discussed in a consideration of the symptomatology of the particular morbid condition to which they are related. But these secondary or symptomatic gastric disturbances—they may be either organic or functional—may in some

cases become so prominent in the symptom complex as to overshadow altogether the primary disease. On the other hand, alterations in the stomach may be regarded as secondary to such primary disturbances as appendicitis or cholecystitis, when, in reality, the original lesion is in the stomach, and many appendectomies and cholecystectomies have been undertaken when only hyperchlorhydria, or gastric or duodenal ulcer was present.

While the majority of serious organic diseases present some symptoms referable to the stomach, we are accustomed to speak of secondary stomach diseases only when marked gastric phenomena are in evidence to direct our attention to the involvement of that viscus. Often these gastric symptoms appear so closely related to the primary affection that it is difficult to decide whether they preceded or were coincident with it. Though cholelithiasis is often accompanied by disturbances in gastric secretion, cases have been reported (J. Kaufmann, A. G. Gerster) which seem to give strong evidence of a cholelithiasis which developed because of preëxisting hyperacidity in the stomach, which caused irritation of the gall-ducts by the passage of hyperacid chyme, thus setting up inflammatory conditions. Study of the functional and chemical processes as they are being actively carried on in the antrum pylori and the duodenum is now more easily possible through the employment of the *gastroduodenal tube* devised by Barsony and Egan, the use of which has greatly increased the possibilities of exact diagnosis of conditions existing in that part of the alimentary canal.

Morbid conditions in which secondary participation of the stomach is in evidence may be discussed under the following classification:

1. Those conditions wherein there is an anatomical involvement of the stomach, immediate or consecutive, due to an extrinsic process secondarily affecting it; for example, perigastric or peripyloric adhesions, constrictions, tugging, etc.; pericholecystitis, subphrenic abscess, tuberculous, carcinomatous, or polyserositic peritonitis, tumor and similar conditions.

2. Those conditions in which not the stomach itself but its nervous supply is anatomically involved, either directly or indirectly. This may be due to pressure, as when the vagus or the sympathetic, in either its cerebrospinal or peripheric course, is imbedded in a tumor, or spinal irritation causes a gastric crisis—both instances of direct involvement. Indirectly, the stomach may be affected by a brain tumor, which acts through intracranial pressure.

3. Diseases having their site in some distant organ often cause grave manifestations in the stomach; for example, kidney disease with renal insufficiency such as uremia, in which the compensatory elimination of the retained metabolic products through the stomach glands provokes the most alarming gastric symptoms. In cases of pernicious anemia, leukemia,

pseudoleukemia, scurvy and hemophilia—bleeding will often take place in the stomach.

4. Congestion of the gastric mucosa which may occur as a consequence of general or local circulatory disturbance, such as venous hyperemia in broken cardiac compensation, or disturbance of the portal circulation.

5. Referred pains of the stomach; for example, in croupous pneumonia, or the radiating pains of appendicitis, cholecystitis, or other abdominal diseases which have their point of greatest intensity in the stomach region (Head's zone of hyperalgesia).

6. Reflex stomach symptoms transmitted through cerebral paths from the peritoneum (genital affections), or produced by toxins due to intoxications and infections; for example, infectious febrile diseases, appendicitis or pulmonary tuberculosis. Stomach symptoms are often set up by irritation of the vomiting center.

7. General diseases which do not especially affect the stomach often display some symptoms which are referable to that organ. Among these may be mentioned loss of appetite, poor digestion, and a sense of pressure in the epigastrium, phenomena often appearing in infectious, metabolic and blood diseases, or in the cachectic state attending malign tumors or other debilitating constitutional diseases.

The differentiation between primary or secondary diseases of the stomach is of prime importance. The first attack of an acute catarrhal appendicitis often takes the form of acute indigestion, with nausea and vomiting but no accompanying rise of temperature, although fever may set in on the second or third day. As the pain may be localized in the epigastrium and we have no history of a previous attack, our attention is likely to be centered on the stomach, and the appendix altogether overlooked. An objective examination will, however, reveal the typical localized tenderness over McBurney's point, and assist in establishing a correct diagnosis and the indications for operation. In such a case, although the patient's complaints are all of the stomach region, the gastric disturbances are only of secondary significance.

In another case, however, precisely similar symptoms, vomiting, epigastric pain, slight fever, tenderness at McBurney's point with marked muscular rigidity, and a history of previous similar attacks, naturally pointing toward a diagnosis of recurrent appendicitis, there were no indications suggestive of any renal involvement. Yet, although there was no pollakiuria, no burning pains during micturition, no backache over the kidney region, nor other suggesting symptoms, the urine passed in our presence contained blood and albumin, proving the existence of nephrolithiasis, producing those recurrent attacks of pain which had simulated those of appendicitis, the gastric symptoms being merely secondary to the primary renal disease.

As these two instances plainly show, the greatest care is necessary in establishing a correct diagnosis, and it is only by minute scrutiny of every indication and careful comparison of all possible points of similarity and difference that we can hope to avoid error. The examination should never be limited to a restricted area like the stomach, but the analysis should be sufficiently extensive to cover all likelihood of secondary involvement, however remote. Observance of these precautions would prevent many unnecessary operations, and also aid in the establishment of the correct diagnosis early enough to permit the choice of the best mode of operation, should this prove to be necessary. Moreover, the treatment of secondary gastric affections will be much more effectual and thorough, with correspondingly more satisfactory results, if their relation to the primary cause of disease is promptly established and fully understood.

As J. Kaufmann has emphasized, the question as to primary or secondary significance—especially in cases of gastric, appendicular and cholecystic involvement, which may be very closely interrelated with each other—may often be exceedingly perplexing. There are cases in which these conditions are present but not in subordinated relation; they are coordinated manifestations of a general spasmophilic condition, which in turn may later play a causative rôle in provoking attacks of appendicitis or cholelithiasis, when at an earlier stage there are no primary pathologic processes in the appendix or gall-bladder, these organs being affected only by spastic contraction.

If operation performed in such cases stops pains and other complaints, it conclusively does not prove more than the result of severing ramification of autonomic nerves and, by this, interruption of the reflex arch (J. Kaufmann).

SIGNIFICANCE OF X-RAY EXAMINATIONS ON THE PATHOLOGY AND THERAPY OF GASTRIC DISEASES

The reasons for considering the significance of X-ray examinations of sufficient importance to be discussed in a separate section are as follows:

1. A brief summary of our present knowledge of the X-ray diagnosis in stomach diseases should prove acceptable in many quarters. Radiology formed no part of the curriculum under which the earlier generation of physicians was educated, and, notwithstanding the fact that many of these older men have—by dint of self-imposed study and practice—acquired the ability to interpret X-ray findings and to correlate them with clinical observation, their knowledge has perforce been gained in a somewhat haphazard manner, and their interpretations are consequently often unsatisfactory. Though the younger generation is better off as regards systematic

instruction in the interpretation of X-ray findings, the majority of practitioners have relatively few opportunities to follow the art, as outside of hospital work roentgenology is employed exceptionally rather than as a routine; and though there are a number of good books on X-ray diagnosis, most of them are so technical as to be useful only to those who devote their entire attention to this work.

2. A better understanding and interpretation of X-ray findings would prevail if the terms used by radiologists were to be systematically taught and known.

3. All therapy is based on diagnosis. At present a most important means to establish a diagnosis is given by the X-ray examination. In certain conditions—notably grave gastric diseases—it is indispensable.

4. Though the primary diagnosis of many conditions can be readily made without the aid of roentgenology, this means is often of the greatest assistance in the interpretation of confusing or atypical symptoms and the settlement of doubtful points. For example, in cases of carcinoma, the precise location, size and advancement of the growth can often be ascertained; or the character and depth of an ulcer—whether penetrating or perforating—can be exactly determined; diagnostic refinements which are of the utmost importance in deciding the question of operability.

But valuable as the X-ray has proved to be in the diagnosis of gastric conditions, we must always guard against too implicit faith in its value, and exercise a due conservatism in our interpretation of its findings. The X-ray has now been in use long enough to enable us to make a just estimate of its worth, so that we neither expect the miraculous nor are skeptical of everything it produces. We fully realize that its chief value lies in using it in connection with the diagnostic data obtained by the other methods of examination at our command: the carefully elicited history, the thorough physical examination, and the examination of gastric contents. As a confirmation and corroboration of such findings it is inestimably valuable; used alone it is not infrequently worse than useless. For example, simple ulcer of the stomach which cannot be visualized by X-ray is easily demonstrated by clinical methods; likewise cancer of the stomach, which is not alone unrevealed by X-ray in about 25 per cent of the cases, but also is not seldom erroneously interpreted upon the X-ray plates, only to have its existence disproved by later clinical findings.

Too much emphasis cannot be laid upon the importance of leaving this work in the hands of specialists who devote their entire time, energies and educational attainments to it. When X-ray work is done by those who have not thoroughly mastered the technic or the art of interpretation it is of little or no use, and we shall be better off to abandon it entirely, and rely wholly upon clinical observation, as did those physicians who lived two or three decades ago. To cite but a single instance of the harm which

may be done by careless and incompetent X-ray work: in many appendectomies, performed after a radiologic diagnosis had been made, the operative findings have reversed those of the radiologist, and the *status quo ante* condition of the patient has proved the diagnostic mistake, all of which might readily have been avoided by a right X-ray diagnosis in time.

The relative merits of *fluoroscopy* and *radiography* is a matter yet much discussed, and the superior advantages of either method are still contested by some radiologists. Yet it would seem as if, at this late date, no such question could possibly arise. Both procedures are useful; neither can supplant the other. They should be used to supplement each other in the same manner that percussion and auscultation supplement each other in the physical examination of the chest and heart. In gastro-intestinal work, where peristaltic waves and other movements have been observed, *fluoroscopy* is *more valuable*. Even cinematography cannot yield the same amount of information as can be gained by a few seconds' observations upon the flouroscopic screen. We are in full accord with Carman when he says:

"I believe that the advantages of the screen in the examination of the digestive tract can hardly be too strongly emphasized. Only by its use can exact information be obtained as to mobility and flexibility, the phenomena of peristalsis and antiperistalsis, the nature and permanence of irregularities of contour, and the effects of palpation, respiratory movement and varying positions."

Under normal conditions, the stomach—whether empty or filled with food—cannot be differentiated from the surrounding viscera under X-ray observation. To make such differentiation possible, it is necessary to prepare the stomach so that it becomes either more or less penetrable to the X-rays than are the structures immediately adjacent to it. By inflating the stomach with gas it becomes more penetrable; by introducing some contrast material, it becomes less penetrable. Practical value attaches only to this latter procedure and it has been universally adopted.

The first attempt to make the stomach impenetrable consisted in giving small quantities of opaque salts in capsules (Strauss, Levy-Dorn, Boas, etc.), but it was not until Rieder administered a voluminous bismuth meal, which completely filled the stomach and made its outlines distinctly visible, that X-ray study of the normal and pathologic processes carried on in this viscus became possible. Rieder first employed bismuth subnitrate, 30 to 40 gm. mixed with 400 gm. of vehicle, but as some fatalities occurred which were attributed to intoxication with this salt, bismuth carbonate was substituted in making up the opaque meal, and is now extensively employed for that purpose. The usual X-ray observations upon the stomach are made as soon as the organ is filled with the opaque meal, but for

minute examination of some particular portion—a niche, pocket, etc.—the bismuth is sometimes ingested in small quantity in form of an emulsion. The "swimming-and-sinking" bismuth capsules devised by Fujinami are especially useful in the examination of cases of gastrosuccorrhea or ectasia with stagnation. The "swimming capsule" floats on the surface of the stomach content, while the "sinking" one descends at once to the bottom, so that by measuring the perpendicular distance between the positions of the two capsules as observed by the X-ray, one is able to estimate approximately the amount of gastric contents (gastric juice and retained ingesta). Haudek's *double-meal method* makes possible simultaneous observation of motility and gastric function. By this method two Rieder meals are taken six hours apart. The examination is made at the time of the ingestion of the second meal. This simple method is very valuable and is now widely used.

In place of bismuth carbonate, pure barium sulphate has more recently been employed in the preparation of the opaque meal (Albers-Schoenberg, Schlesinger, Carman and others). It offers the double advantage of far lower cost and perfect harmlessness, and passes through the normal stomach in about four hours, while the passage of the bismuth meal requires six hours.

There has been much discussion as to whether any opaque meal can produce conditions in the alimentary canal identical with those attending the passage of ordinary food taken in a normal way. The opaque salt is heavier and bulkier than normal food substances, and the vehicle is often distasteful to the patient, so that the opaque meal is taken with aversion and fails to exert the normal stimulus upon the mucous membrane of the stomach. This view found the most resolute spokesman in Stiller, but the consensus of opinion now is that for all practical purposes the opaque meal serves to demonstrate the conditions—physiological or pathological—which prevail during the passage of ordinary palatable food. Both bismuth and barium salts are suited for X-ray work, for not only do they absorb rays and cast distinct shadows, but, being heavy metallic salts, they will settle upon the surface of a tumor, or sink to the pit of an ulcer, encrusting a denuded surface even after the mass of the meal has passed on, so that gastric residue, niches or pockets can thus be plainly visualized. In this covering and protective property also resides the therapeutic value of the administration of these two salts (for bismuth, Kussmann, Fleiner; for barium, Galambos).

Observation of the Normal Stomach.—X-ray observation of the passage of Rieder's bismuth meal gives us information concerning the location, size and shape of the stomach, the localization of pain or tumor, passive mobility, muscular tonus, peristalsis, motility, hypersecretion, the presence of new growth or ulcer (filling defect, niche, accessory pocket), perigastric adhesions, extrinsic compression or tugging.

As soon as the bolus has passed the cardia we can make our first observation—the *tonicity of the stomach wall.* When the entire meal has passed the cardia we can observe the form of the stomach. Tonicity and form are closely related to each other. The *fishhook* form was that observed by Rieder in the great majority of normal individuals, while Holzknecht described the *steer-horn* type as being most often present. Schlesinger classified the "normal shapes," differentiating the hypertonic, orthotonic, hypotonic and atonic forms, the most common being the orthotonic. What he designates as hypertonic resembles the form described by Holzknecht, while the others approximate Rieder's type. The form of any given stomach is more or less dependent upon the constitutional make-up of the individual, and can only be considered in its relations to the other anatomical findings. The plethoric man of apoplectic habitus is likely to have a short, downward tapering stomach of the Holzknecht type, lying high and nearly horizontal without the long vertical pars pylorica, the pylorus being the lowest point. The stomach harmonizing with the asthenic habitus (the asthenia universalis congenita of Stiller) will be of the hypotonic and atonic form (Rieder's fishhook stomach) characterized by the elongation and perpendicular position of the upper two-thirds, and a sharp angle formed by the lower third on the lesser curvature at the juncture of the pars media and pars pylorica, so that the pylorus curves upward, and the lowest point is at the greater curvature. The long vertical pars pylorica is always present; the median diameter will be the largest and the cardiac diameter the smallest.

Pfahler describes the *position* of the normal stomach as follows:

"It occupies the left side of the abdomen and extends from the inner two-thirds of the left side of the diaphragm to the median line, usually about an inch above the umbilicus. The upper two-thirds is almost vertical and the lower third almost horizontal, making the general direction of the stomach somewhat oblique. The pyloric portion extends from one to two inches beyond the median line to the right."

The *size* of the stomach varies according to the amount of food intake, though its muscular tone, shape and position also have an influence upon its size. It is never necessary to gage exactly its maximum capacity. Schlesinger considers of normal size a stomach which is filled by the 400-gm. bismuth meal, while Carman expects an adult orthotonic stomach to accommodate a 700-c.c. bismuth meal. Other observers give still more widely divergent estimates of the capacity of the normal stomach.

The free *passive mobility* of the stomach, as well as the free *flexibility* and *pliability* of its walls, can easily be demonstrated in the normal organ. Deep respiration and active contraction of the abdominal wall by the subject under examination, or palpation by the examiner, will bring about

changes in form and contour, though these are more readily perceived upon an elongated stomach than when we are dealing with an organ of the steer-horn type.

By the *tone* of the gastric musculature we mean its capacity to contract upon and adjust itself to its contents (Carman). Stiller uses the term "peristole" for the determination of the tone of the gastric musculature. The degree of tonus is determined by the tension of the tissues, especially their elastic and muscular elements. The innervation, or the tonus due to innervation, is reflexly maintained, and is an indication of the subject's general constitutional state. As the pneumogastric nerve has the principal rôle in this innervation, any change in vagus tonus will bring about a corresponding change in gastric tonus. Shape and tonus are closely related, for the *shape* of the stomach is largely determined by the *tone* of its musculature. In the asthenic habitus, we ordinarily find lessened tonus; if atony is encountered, it is generally regarded as a sign of constitutional inferiority.

Peristalsis is the active motility of the stomach, the name being applied to the muscular wave which moves downward from the upper two-thirds of the stomach to the pylorus, progressing in regular rhythm. An entire peristaltic wave is also termed "peristole" (Kussmaul), but this should not be confused with the same word as applied to the determination of gastric tonus by Stiller. Peristalsis is more intense along the greater curvature. The direction of the waves is perpendicular to the long axis of the stomach. Over the middle of the stomach the waves are rather shallow and wide, but as they approach the pylorus their depth and intensity increase. At the pyloric third the peristaltic wave is changed into a deep *contraction ring,* the *sphincter antri pylori,* which cuts off the antrum pylori from the upper and larger, proximal portion of the stomach. This deep contraction ring moves toward the pylorus (propulsion), the size of the antrum meanwhile gradually diminishing until it has entirely disappeared. The pylorus being closed, propulsion and contraction of the antrum pylori serve but to cause a backflow of the ingesta from the antrum into the stomach proper; only when the pyloric ring relaxes can a relatively small portion of the stomach contents pass through it.

Pyloric opening is influenced by several factors, among which are the strength of peristalsis and the quantity and acidity of the stomach contents, the muscular tone of the pylorus itself, the filling condition of the stomach, the condition of the intestines, and finally the state of the vegetative nervous system. Kaufmann and Holzknecht estimated the average duration of a peristaltic wave at twenty-two seconds, and the interval between the waves as about twenty seconds. Peristalsis begins the moment the first food portion reaches the pylorus. In atonic conditions it may commence after the ingestion of the third or fourth bolus. The presence of solid material at the pylorus is all that is necessary to

induce peristalsis, but it is not set up by gas or fluid. By peristalsis thorough mixing and evacuation of the stomach contents is effected in both parts but in a different manner and degree. Antrum and stomach are separated by the contraction ring, representing, according to Hofmeister and Schultz, locally separated and functionally different parts.

Observations of Pathological Conditions.—The size of the stomach may pathologically be increased or diminished. Enlargement or diminution does not of itself signify disease, but, when associated with other symptoms, it may prove a valuable help in establishing diagnosis.

Small stomach to a certain extent may be encountered in normal individuals, as when the X-ray shows that we are dealing with the steer-horn stomach of Holzknecht, regarded by Schlesinger as a hypertonic variation of the normal type. Small stomach is observed in all cases of hypertonus. The lumen is decreased in the presence of any form of tumor; in medullary cancer, the inward-bulging tumor reduces the space within the stomach, while diffuse scirrhous infiltration of the stomach wall lessens the gastric capacity by causing thickening and rigidity of the wall with subsequent shrinkage and loss of elasticity.

Enlargement of the stomach may occur when the tonicity of its wall is lessened (hypotonus, atony), according to the nomenclature of Boas, in *ectasia of the first degree.* Ectasia ventriculi (Boas' *ectasia of the second degree*) is always a secondary symptom accompanying anatomical alterations in or around the pylorus, such as carcinoma, ulcer, cicatrix, benign tumor, lues, tuberculosis, peripyloric or periduodenal adhesions, or extrinsic tumors bulging into the stomach or duodenum.

Dilatation is a passive condition, secondary to hypertrophy of the musculature. When muscular action proves insufficient, the X-ray will reveal the ectatic stomach enlarged in all directions, displaced to the right with the right distance increased, and casting a crescentic bismuth shadow. The presence of six-hour residue will be the deciding factor. Ectasia, according to the underlying cause, may be accompanied by tumor, niche, pocket; extrinsic tugging, reversed peristalisis, hypersecretion, or pylorospasm.

The *shape* of the stomach is—as we have already noted—normally subject to considerable variation and, under pathologic conditions, this variance may be greatly increased. In determining whether the observed shape is physiological or pathological, we must take account of the subject's age, sex, and general constitutional state. The Holzknecht type (steer-horn) is found only in broad-shouldered individuals of hypersthenic habitus. The Rieder type (fishhook) is that more commonly found when conditions are normal; while the stomach, the hypotonic and atonic stomach, is more common in the habitus designated by Stiller as asthenicus universalis. If we find a steer-horn stomach in an individual of asthenic

habitus, it is just as much indicative of disease as the observation of a fishhook stomach in a patient of hypersthenic build.

Widely varying shapes may be assumed by the stomach under the influence of the different pathological process which may take place in or around it. Not only do we see the forms produced by atony, ectasia or ptosis, but also those diverse shapes which are due to the presence of tumors or ulcers at the pylorus, as well as the condition known as hour-glass stomach, snail-form with acute flexion of the pylorus, or still other shapes induced by torsion, compression, adhesion, or accretion. The shape of the stomach is likewise largely dependent upon its situation. Secondary or reflex functional disorders—the primary focus of which is located in some other organ—affect the gastric musculature and thus the shape of the stomach too.

The *situation* or *position* of the stomach may indicate that the viscus has undergone marked alteration, largely because of changes in its size and shape. Its position may be altered by the attachment of external accretions or "pseudoligaments," by other tugging, or it may be fixed by perigastric adhesions, or attached to the duodenum or gall-bladder in such a manner that the pyloric end will be displaced upward, and to the right side. Shrinking of the tissues around a chronic calloused ulcer of the lesser curvature may drag down the lower part of the stomach, producing the snail-form, or what is sometimes termed "cascade-form." While such anatomical changes affect only one section of the stomach, gastroptosis will have an influence upon the entire organ, and may cause it to sink so low that the greater curvature will be found within the pelvis.

The *mobility* or *passive mobility* of the stomach can be either wholly or partially suspended, and alterations in its mobility may be observed by contraction of the abdominal wall, or by massage or pressure by the palpating hand. Factors able to lessen the stomach's mobility are external fixation from any cause, accretion, neoplastic infiltration, or the contraction of cicatricial tissue following ulcers, etc. *Hypermobility* will be found in an elongated, freely movable stomach (ptosis, atony).

Localization of pain (in gastric ulcer) and *tumor* (carcinoma) can only be accomplished by the employment of the fluoroscopic screen.

Alterations in muscular tonus: An increase in the tone of the muscular wall is termed *"hypertonus"*; a lessening of this muscular tone we call *"hypotonus"* or *"atony."*

Hypertonus—up to a certain degree—is sometimes present in normal individuals, notably those of apoplectic habit, with a high-lying steer-horn stomach having its largest diameter in the cardiac region, and tapering to the pylorus, which is at the lowest point, no long vertical pars pylorica being present. The wall of such a stomach will be greatly contracted and closely molded about its contents. Such hypertonus, which may present a normal variation under morbid conditions, in a more pronounced form

will give us *pathologic hypertonus,* often a secondary or reflex symptom of disease elsewhere in the body; for example, duodenal ulcer, which is often observed in conjunction with hyperperistalsis and hypermotility (*duodenal reflex-neurosis* of E. Schlesinger.)

Hypotonus or *atony*—lack of tonicity—is a condition more frequently encountered. The atonic stomach is of Rieder's fishhook form and, as this is the type found in the majority of normal individuals, it is often difficult for the observer to decide whether he is presented with normal or pathological conditions. When tonus is lacking the stomach wall does not contract sufficiently to mold itself about the ingesta, so that the food drops—as it were—into an empty sack, and, the stomach being fixed at its cardiac and pyloric ends, the center becomes overloaded and the median diameter greatly increased while the cardiac diameter is so decreased as to almost disappear. The long vertical pars pylorica becomes greater, thus enhancing the impaired motility due to atony, and this, in turn, serves to increase gastric dilatation. The gas bubble is large and often irregular in shape. Atonic symptoms are present only while the stomach contains ingesta. As soon as it is emptied of its contents the musculature will contract again (Kuttner) and the surgeon and anatomist do not find any signs of atony.

Atony should not be regarded as a pathologic entity, but only as a manifestation of a constitutional shortcoming. Conditional moments play very little, if any, rôle in bringing it on. It is often associated with loss of muscular tone all over the body, and will be observed in conjunction with splanchnoptosis, constipation, venectasia, varicocele, flatfoot, hyperextensibility of the joints, faulty posture, etc. Atony of the stomach is sometimes confused with gastroptosis, a condition with which it is very often present. Both states are due to constitutional inferiority, but in gastroptosis the entire stomach is lowered. Pyloroptosis (Groedel) is present as a sign of the general splanchnoptosis, although the height of the pyloric opening above the lowest point on the greater curvature is not necessarily increased. The cardiac, median and pyloric diameters of the stomach will be found almost equal, and the curvatures remaining so nearly parallel as to give the organ the appearance of a long curved tube. In ectasia of the stomach it is of prime importance to note any increase in the right distance (Groedel-Faulhaber); ectatic enlargement affects all diameters, and the shadow cast by the bismuth meal will be of crescentic form.

If peristalsis be pathologically increased, it is termed *"hyperperistalsis";* if lessened, *"hypoperistalsis." Hyperperistalsis,* which is of the greater interest and significance, is often indicative of the existence of muscular hypertrophy in the stomach. Muscular hypertrophy—if existing for an extended period—will increase peristalsis in the stomach, in the same manner as, in the heart, the biliary tract, or the urinary canal; we

find increased peristalsis when some anatomical or pathological obstruction prevents the evacuation of a hollow organ. The hindrance to evacuation may vary in character: it may be a cancer or benign tumor, an ulcer, or the cicatrix of an ulcer, peripyloric adhesions or other accretions, or an extrinsic tumor, pressing upon the lumen of the stomach from without. Yet we must not forget that very often, in carcinoma of the stomach with marked pyloric obstruction, we may see retarded peristalsis, with shallow and infrequent waves of unequal intensity sometimes followed by reversed peristalsis.

Hyperperistalsis does not necessarily mean increased or accelerated evacuation, at least in those cases where anatomical lesions exist. On the contrary, under these circumstances hypertrophy and hyperperistalsis are compensatory processes, indicating that the stomach is adapting itself to the presence of the obstruction. Hyperperistalsis developing in the absence of stenosis, as a secondary or reflex symptom of the excitomotor function of the stomach, in cases of functional disorder (neurasthenia, hysteria, tabes dorsalis, achylia gastrica, etc.) or—especially—in cases of duodenal ulcer, may be accompanied by hypermotility. The impulses will take place with increasing frequency—the intervals between them being lowered up to ten seconds. When the time of broken compensation approaches and the hypertrophied musculature proves unable to combat the obstruction, secondary dilatation will set in, with marked decrease in motor power. The exhausted muscles can no longer produce hyperperistalsis, and hypoperistalsis takes its place. When symptoms of stagnation appear the digitalis of this motor insufficiency is the systematic lavage of the stomach or gastro-enterostomy.

When hyperperistalsis is present the waves are deep and concentric, cutting through the entire lumen, and following one another with such rapidity that a new wave arises before the preceding one subsides, so we may see two or even three or more peristaltic waves in action at once. This is a typical picture. Such increased muscular activity may develop into tonic contraction, thus producing spastic incisura, pylorospasm, etc. The wave starts high up in the cardiac region and, if peristalsis is greatly exaggerated, the increased muscular activity can be palpated or even observed through the abdominal wall; manifestations called "stiffening" of the stomach accompanied by syringe sound.

A special localized pathologic manifestation of hyperperistalsis is the spastic contraction of the greater curvature on a level with the site of an ulcer or cancer. This *incisura* is a finger-shaped indentation, in ulcer cases deep and narrow, producing the spastic form of hour-glass stomach; while in cancer cases it is wide and relatively shallow. The incisura may disappear when the patient is being examined before the screen, if antispasmodics (atropin, papaverin) are administered.

Hyperperistalsis may lead to a manifestation, called *pylorospasm,* a

tonic spastic contraction of the pyloric ring. This is always a secondary manifestation, met with where there is present a special constitutional disposition (spasmophilia) or, in cases of ulcer, cholelithiasis, hypersecretion and hyperacidity, or impaired motility. Under such conditions we find a vicious circle, for pylorospasm serves to increase the motor insufficiency and promote still greater secretion and acidity. With the patient before the screen, spasm of the pylorus may be abolished by the use of antispasmodics. Hyperperistalsis does not necessarily indicate hypermotility; in cases of anacidity or achylia gastrica, they are both present, while the administration of hydrochloric acid will increase peristalsis, but lessen gastric motility.

Diminished peristalsis will be observed in the second stage of pyloric obstruction after passive dilatation has set in. Schlesinger found that the direct tactile stimulus of solid food within the stomach cavity is necessary to provoke peristalsis. In cases of maximal hypersecretion, when a zone free of "contrast meal" is between the bismuth mass and the stomach wall, there will be no peristalsis. The stomach of the milk-fed infant showed no peristalsis (Flesh-Petery), but, as soon as solids were ingested, peristalsis was set up. No peristaltic waves are visible in a stomach inflated by gas (Roll, Roepke), and, according to Tabora and Dietlen, oil administered for therapeutic purposes in pylorospasm immediately stopped peristalsis, the pylorus remaining wide open.

When pyloric stenosis exists—no matter from what cause it may arise—the peristaltic waves, even if hyperperistalsis is present, will not be able to bring about evacuation of the ingesta into the duodenum. When the impulse of the normal peristaltic wave is exhausted at the pylorus, a reverse action may take place—the so-called *antiperistalsis* or *reversed peristalsis.* This consists of a series of regular waves, usually wider and more shallow than the normal, having their origin at the pylorus and retrogressing in constricting wave-form toward the middle of the stomach. Reverse peristalsis is usually more marked upon the greater curvature. As the normal peristaltic movement is unable to pass the ingesta through the pylorus it is obvious that the stomach contents will be forced back. This backflow, however, is a rather passive movement, and the periodic bulging of the stomach wall which follows it in retrograde wave-form, is likewise a passive process (Schlesinger). The ingesta, thrown upon the stenotic pylorus, rebound and are regurgitated from the antrum pylori into the median portion of the stomach. During this periodic to-and-fro movement of the ingesta, peristalsis and antiperistalsis usually alternate, the reverse impulse originating where the normal wave expires.

Antiperistalsis is seldom found save in cases of organic pyloric stenosis (Schlesinger, Carman) due to cancer, ulcer, scar formation, or outside adhesion or compression. Its significance as an early sign of pyloric cancer has not been firmly established; Jonas found it, in its early stage,

in cases where stiffening of the stomach wall was observable. Some observers claim to have seen reversed peristalsis when no organic lesion was present (tabes, neurasthenia), but as yet this finding has not been satisfactorily corroborated. Antiperistalsis is, however, a very valuable symptom, as its presence is strongly indicative of some organic lesion probably calling for operative intervention.

Too rapid emptying of the stomach is termed *"hypermotility"*; opposed to this we have retarded emptying or *"hypomotility,"* the extreme degree of this condition being found in *complete obstruction.* In X-ray diagnosis, the motor function is expressed and characterized by the length of time necessary for a full evacuation of the stomach. The normal time required for passage of the bismuth meal is six hours, the barium meal passes in about four hours. A six-hour residue indicates impaired motor function, and an eight-hour residue is almost proof positive of an organic pyloric stenosis. In cases of hypermotility, on the other hand, there is rapid gastric clearance, the duodenal cap is quickly filled out, and in a few minutes evidences of the presence of bismuth in the intestines may be observed. Though often associated with hypertonus and hyperperistalsis, hypermotility does not necessarily occur in conjunction with them; in duodenal ulcer we commonly observe all three conditions, but in ulcer of the stomach hypomotility (pylorospasm) is often present. In gastric cancer, when the growth is at some distance from the pylorus, hypermotility is a common finding, while when the cancer is located in the pyloric region motility becomes impaired. Atony may be associated with hypermotility too in cases complicated by achylia gastrica.

Not all cases of pyloric cancer display impaired stomach motility. Although in cases of pyloric cancer that orifice may be obstructed with resulting stagnation of the stomach contents, it will sometimes be found gaping wide open, with consequent hypermotility of the stomach. The pylorus will remain open in those cases of cancer where an infiltrative mass prevents its closure, or in cases of medullary cancer where the process is far advanced; the new growth which at first obstructed the outlet will necrose and fall off, thus leaving the orifice open. Delay in stomach clearance may also be due to reflex action of functional or organic disease in other parts of the body, by which the motor power of the stomach may be disordered, either indirectly by spasm of the pylorus or hypersecretion, or directly, as it may happen in hysteria, neurasthenia, tabes, cholelithiasis, appendicitis, or diseases of the genital tract. The ingestion of hydrochloric acid delays motility by increasing pyloric tonus; alkalis and antispasmodics increase it; oil stops peristaltic action, but opens the pylorus; emptying of the stomach contents is greatly retarded, but it can also be accelerated; if the patient lies on his right side, evacuation will be accelerated in a "passive way" by permitting passage through the gaping pylorus to be accomplished by gravity.

Hypersecretion—Residue.—The X-ray is principally useful in demonstrating motor disturbances and the presence of anatomic lesions; disorders of secretion must usually be studied by the aid of the stomach tube. While we cannot directly detect qualitative disorders of secretion by X-ray observation, quantitative disorders due to hypersecretion may produce signs which can directly be demonstrated by means of the X-ray. In cases of hypersecretion, between the "contrast" material and the gas bubble, we can perceive an intermediate translucent stratum, bordered by horizontal lines. If there is a high degree of hypersecretion the bismuth meal may be noted to be suspended in this wall standing fluid. If hypersecretion is continuous, the swimming bismuth capsule ingested by the fasting stomach will swim over the surface of the fluid, and, as has been already noted, the distance between the swimming and the sinking capsule will give an approximate measure of the quantity of fluid or residue, although the X-ray does not permit us to distinguish between a hypersecretion of fluid and a food residue.

Direct Signs of Organic Lesion.—In addition to the alteration in form, size and motor power, etc., which have been enumerated above, we can demonstrate the presence of actual lesions, tumors, ulcers, etc., by *direct* signs by means of fluoroscopy, and even better by means of radiography. Altered tonus, peristalsis, motility, mobility, and so on, are usually secondary or *indirect* signs, likely to be present in widely varying conditions, in the presence of organic diseases, or as reflexes of functional disorders, and, therefore, have only the value of confirmatory symptoms. We have, however, direct signs, typical of organic lesions, which are pathognomonic, and make possible the establishment of a complete diagnosis even when no other symptoms are available. Direct signs for cancer of the stomach are: filling defects (Holzknecht and Jonas). Direct signs for ulcer of the stomach are: niche, accessory pocket (Haudek) and hour-glass stomach (organic).

Filling Defects.—A break in the normal outline of the shadow of the contour of the stomach, when occurring over a circumscribed area, is called a filling defect. It is the *negative* of a tumor shadow, a *relief* of the inner surface of the tumor, bulging into the lumen of the stomach. This projection will display indefinite edges and an irregular uneven surface, sometimes indicative of the location of the crater of its central ulceration. A marked characteristic is that the involved area will not show any peristaltic movements, the waves stopping at the edge, skipping over the defect, and appearing again beyond its distal limit, and no outside agents—drugs, massage, reëxamination, etc.—will suffice to induce peristalsis in the affected area. Because of the great frequency of gastric cancer in the pyloric region (90 per cent in the Mayo Clinic), filling defects are most often observable in the pyloric third of the stomach. The filling defect corresponds to a tumor mass which can be palpated if it happens to be

located within reach of the examining hand, and it has been frequently observed that a tumor which has escaped the hand of the clinician can be recognized and palpated by the roentgenologist when he has his patient in the upright position before the screen.

Outlines similar to those due to a filling defect can sometimes be produced by several other disturbing causes and the possibility of confusion should be kept in mind. Indentation of the greater curvature is sometimes due to a gas-filled colon. The irregularity caused by the intrusion of an extragastric tumor is usually rounded.

The establishment of the exact location of a filling defect has much more than merely academic value, as the question of operability must be answered in view of this point. If the filling defect is in the pyloric third, the tumor is operable; if it is located in the pars media, the chances of operation are "border line," that is, doubtful or uncertain; while a tumor located in the cardiac portion of the stomach is usually not amenable to surgical intervention (Carman).

Not only is the filling defect the surest and most pathognomonic sign of gastric cancer; it is also the one we are most frequently able to observe. Though X-ray operators often affirm that not more than from 75 to 78 per cent of gastric cancer cases can be positively diagnosed, Carman reports from the Mayo Clinic that 95 per cent of their gastric cancer cases gave signs distinctly visible by X-ray. Moreover, filling defect is an earlier symptom than motor insufficiency, hematemesis, etc.

Not alone the location but the size of the filling defect, and its character—whether that of scirrhous infiltration or the circumscribed proliferation of the medullar form—are of prime importance both diagnostically and therapeutically in deciding the possibility of operation. Not infrequently carcinoma of the pylorus will manifest itself not by a filling defect, but by deficiency of the entire pyloric region, and the shadow of the contrast meal will terminate with a sharply defined edge around the median and pyloric third.

Niche—Accessory Pocket.—In the same way that the filling defect is characteristic of gastric cancer, the niche and the accessory pocket are pathognomonic of ulcer of the stomach. All roentgenologists agree that ulcus simplex, that is, ulcer in the acute stage, gives no *direct* sign. Different opinions prevail in regard to secondary signs, Faulhaber maintaining that acute ulcer has no influence on the motility of the stomach, while Haudek reports that ulcus simplex is accompanied by pylorospasm and a repeatedly demonstrated six-hour residue. The direct ulcer symptoms are those caused by the presence of the chronic infiltrative type (ulcus chronicum callosum). In accordance with the depth of the ulcer we designate the defect as *crater, niche* or *accessory pocket.* The crater of a chronic ulcer is roentgenologically revealed as a permanent spot. A deeper excava-

tion where there is actual burrowing into the stomach wall will show a deep crater-like diverticulum, jutting out from the lumen of the stomach, but with no perforation of the serosa, and is called "ulcus penetrans"; the crater visualized is the *niche*. When complete perforation has taken place into a formerly accreted organ or peritoneal conglomerate, the ulcer is called "ulcus perforans," revealed in the picture by the presence of an *accessory pocket*. The first X-ray picture of an ulcer crater was made by Reiche; later the subject was more thoroughly studied by Haudek, who described the niche, applying this designation, however, to both the penetrating and perforating types.

The *niche* is properly a budlike prominence springing from a broad base and jutting out into the lumen of the stomach the full width of this base. The *accessory pocket* shows a short narrow column, which often cannot be visualized, when the pocket looks beside the stomach "like an isle in the sea" (Schlesinger). While the niche is filled by the opaque meal, in the accessory pocket we sharply differentiate three layers: the shadow-casting bismuth mass below, above this a more translucent fluid stratum, and on top a cap of gas bubble. No massage or other manipulation can dislocate the bismuth or push it out of the pocket, and it may occur that when the patient assumes a recumbent position or lies on the side and the gas bubble escapes, its place will immediately be filled up by the bismuth mass. It is characteristic of these symptoms that when we are unable to visualize them distinctly, by turning the patient on the right side, they sometimes may become plainly evident at once. This is because the common site of gastric ulcer is on the lesser curvature. It is often equally effectual to press the bismuth mass by means of our palpating hand through the abdominal wall into the upper region of the stomach, or sometimes when the patient is turned sidewise before the screen. The peristaltic waves will be observed to stop when they reach the indurated and shrunken tissue around the ulcer, as they do on reaching the filling defect caused by the presence of cancer.

The X-ray picture shows not only the existence of chronic ulcer, but enables us also to see its location, extent and character (penetrans or perforans), and—in cases of perforating ulcer—whether it has caused adhesion to other organs, or has actually invaded them. Therefore, in addition to diagnostic aid, the X-ray can assist in deciding the wisdom of operation, the choice of operative methods, and so on. It is important to exercise conservatism in regard to advising operative intervention for, even in ulcus perforans, gastro-entero-anastomosis has not always given absolutely satisfactory results; the mortality attending resection is high, and healing has been known to take place without surgical interference too. There are cases reported in which the clinical symptoms of perforating ulcer have entirely disappeared even when the X-ray picture continued to show unchanged anatomical conditions.

Organic Hour-glass Contraction.—An ulcer developing near the pylorus may in its final cicatricial stage cause hardening and shrinkage of the tissues to such an extent as to set up pyloric stenosis; when the ulcer is located in the fundus of the stomach cicatrization will cause indrawing, sometimes so marked as to draw the walls of the viscus almost together, dividing it into an upper and a lower section, producing what is termed "hour-glass stomach." This abnormality is always plainly visible to the roentgenologist, and in its extreme form can be palpated or even seen through the abdominal wall. The hour-glass stomach caused by the contraction of a scar must be differentiated from that due to functional derangement, which may sometimes be the result of a spastic incisura on a level with a cancer or ulcer. This contraction is not constant, and will disappear if the patient is given an antispasmodic (atropin, papaverin).

REFERENCES

Albers-Schoenberg. Roentgentechnik, 1919.
Albu. Autointoxicationen, Aug. Hirschwald, Berlin.
Aldor, von. Ztschr. f. klin. Med., xl, 248, 1900.
Anderson. Brit. Med. Journ., 1890.
Baibakoff. Arch. f. Verdauungskr., xii, 54.
Bamberger. Behandlung des chron. Magengeschwürs., Verl. Julius Springer, 1909.
Barsony-Egan. Wien. klin. Wchnschr., 1922.
Bassler, A. Diseases of the Stomach and Upper Alimentary Tract, 1923.
Bauer, J. Konstitutionelle Disposition zu inneren Krankheiten, 1917.
Baum. Therap. d. Gegenw., 1902.
Best. München. med. Wchnschr., 1908.
Best and Cohnheim. Deutsche med. Wchnschr. Vereinsbericht, l, 2368, 1910.
Beyea. Journ. Am. Med. Ass., 766, 1910.
Bickel. Deutsche med. Wchnschr., xxxv, 1905; 2368, 1906.
——— Berl. klin. Wchnschr., 1905.
——— Discussion of Schmidt's Paper in Deutsche med. Wchnschr., x, 475, 1911.
Bircher. Corresp. d. schweiz. Aerzte, xxi, 1891 .
Bloodgood. Tr. Am. Gastro-enterol. Ass., 1911.
Boas. Diag. u. Therap. d. Magenkrank.
——— Therap. d. Gegenw., 1904.
——— Deutsche med. Wchnschr., 1903, 1906, 1907.
——— Samml. klin. Vortr. n. F., 387.
——— Magenkrankheiten, 1920.
——— Diaetetik d. Magen u. Darmkrankh., 1920.

Boldireff. Arch. f. d. ges. Physiol., cxxi, 13.
Bouveret and Devic. Rev. de méd., xii, 1892.
Brinton. Diseases of the Stomach.
Brown, W. L., Murphy, J. K., and Allbutt, T. C. Practitioner's Encyclopedia of Medical Treatment, 1915.
Brunner. Deutsche Chir., xlvi, 1907.
Brunton, Lauder. Practitioner, July, 1905.
Busch. Arch. f. klin. Chir., xc, 1.
Cahn, A. Ztschr. f. phys. Chemie, x.
Carman, R. D. The Roentgen Diagnosis of Diseases of the Alimentary Canal, 1921.
Cheinisse. Semaine méd., xxx, 109-120, 1910.
Chiari. Uber Magensyphilis, Festsch. zu Virchow's 70 Geburtstag, 1891.
Clairmont. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xx, 1909.
Cohnheim. Therap. d. Gegenw., 1902.
——— Ztschr. f. klin. Med., lii, 1904.
Croner, W. Therap. a. d. Berl. Univ. Klin., 1920.
Dieulafoy. Clin. méd. de l'Hôtel Dieu de Paris, 1897-1898, ii, 1899.
Donkin. Lancet, 1890.
Einhorn. Med. Rec., June 2, 1892.
——— Phila. Med. Journ., 1900.
——— Diseases of the Stomach, 6th ed., 1920.
Elsner. Lehrb. d. Magenkr., 263, S. Karger, Berlin, 1909.
Eppinger and Hess. Von Noorden's Samml. klin. Abhandl. ü. Path. u. Therap. d. Stoffwechs. u. Ernähr.-Störung., ix, x, 1910.
Erb. München. med. Wchnschr, 1904.
Ewald. Deutsche Klin., v, 508.
——— Therap. d. Gegenw., 1900.
Ewing, J. Neoplastic Diseases, 1922.
Falta, W., Meyers, M. K. The Ductless Glandular Diseases.
Fenwick. Dyspepsia and Its Varieties, W. B. Saunders Co., 1910.
——— Ulcer of the Stomach, 135, P. Blakiston's Son & Co., 1900.
——— Brit. Med. Journ., 1900.
Fleiner. Krankh. d. Verdauungsorgane.
——— Verhandl. d. XII Kong. f. inn. Med., 1893.
——— München. med. Wchnschr, xxiii, 1903.
——— Therap. d. Gegenw., 1904.
——— Verhandl. d. XX Kong. f. inn. Med., 1923.
Fournier. La Syphilis, April, Aug., 1903.
——— La Syphilis, i, 1, 1903.
——— Traité de la syphilis, i.
Galambos, A. Arch. f. Verdauungskr., xvii, 4.
——— Ztschr. f. klin. Med., lxxi, 5, 6; lxxxiv, 5, 6.
——— Wien. klin. Wchnschr., 1920.

Galambos, A. Kriegsepidemiologische Erfahrungen, 1917.
Gerhardt, D. Krankh. d. Speiseroehre u. d. Magens, III, B., 1921.
——— Handbuch der ärztlichen Erfahrungen im Weltkriege, 1914-1918.
Gompertz, Louis M. Tr. Conn. State Med. Soc., 240-245, 1910.
Gross. München. med. Wchnschr., 1903.
Gruber, G. G. B., and Kratzeisen, E. Wesen des Ulcus Pepticum Ventriculi und Duodeni, 1922.
Haas. Therap. d. Gegenw., March, 1905.
Hare, H. A., and Landis, H. R. M. Modern Treatment.
——— Progressive Medicine, 1918-1922.
Harnack. Berl. klin. Wchnschr., xviii, 1888.
Hayem. Rev. de méd., 1889.
——— Presse méd., February 18, 1905.
Heinsheimer. Berl. klin. Wchnschr., 1906.
——— Med. Klin., 1906.
Hemmeter. Diseases of the Stomach, P. Blakiston's Son & Co.
Hemmeter and Stokes. Arch. f. Verdauungskrankh., vii.
Hepp. Gaz. d. hôp., 1903.
Holitsch, R. A roentgenezes tankoenyve, 1918.
Jacobi. Con. Am. Phys. & Surg., Med. Rec., 1897.
Jaworski. Deutsche Arch. f. klin. Med., xxxvii.
Kaller, S. Berl. klin. Wchnschr., xlix, 2189, 1909.
Kaufmann, Jacob. Am. Med., vi., Nov., 1903.
——— Am. Journ. Med. Sc., April, 1904; Feb., 1908; June, 1910.
——— Arch. f. Verdauungskrankh., xiii, 6.
——— N. Y. Med. Journ., 1912.
——— Journ. Am. Med. Ass., 1913.
——— Med. Rec., 1918.
——— Mitt. a. d. Grenzgeb. d. Med. u. Chir., xxxvi, 922, 1923.
Kausch, W. Deutsche med. Wchnschr., i, 8, 1911.
Kiralyfi, G. A belsoebetegsegek therapiaja, 1922.
Klemperer. Therap. d. Gegenw., 1907.
Kocher. Mitt. a. d. Grenzgeb. d. S. Med. u. Chir., xx, 1909.
Krehl. Pathologische Physiologie, 1920.
Kussmaul. Deutsches Arch. f. klin. Med., vi.
——— Samml. klin. Vortr., n. F., 181.
Kuttner. Berl. klin. Wchnschr., 1895.
Lafleur. Montreal Med. Journ., vii, 1903.
Lambert, Samuel. Am. Journ. Med. Sc., Dec., 1904.
Lebert. Krankh. d. Magens, Tübingen, 1878.
Lenhartz. Med. Klin., iii, 15.
——— Deutsche med. Wchnschr., 1904, 1906.
——— XX u. XXVI Kong. f. inn. Med.
Leo. Die Salzäure Therapie, Berlin, 1908.

Leube, von. Arch. f. klin. Med., xxiii, 1879.
——— Penzoldt, Handb. d. spec. Therap. inn. Krankh., iv.
——— Spec. diag. d. inn. Krankh., F. W. Vogel, Leipzig.
——— Deutsche med. Wchnschr., xxii, 1909.
——— Verhandl. d. Gesellsch. f. Chir., 1897.
Lieblein. Deutsche Chir., xlvi, 100.
Lientier. Thèse de Paris, July, 1904.
Lockwood. Journ. Am. Med. Ass., April 1, 1911.
Malbranc. Berl. klin. Wchnschr., 1878.
Martius. Achylia Gastrica, Franz Deuticke, Leipzig, 1897.
Mathieu and Laboulais. Bull. Soc. Méd., 1901.
Matthes. Centralbl. f. inn. Med., 1894.
——— Albu's Abhandl. d. Verdauungskr., ii, 4.
Mayer. Brun's Beitr. z. klin. Chir., vi, 1908.
Mehring. Lehrb. d. inn. Med., 1920.
Meyer. XXIV Kong. f. inn. Med.
Moritz. Ztschr. f. Biol., xlii.
Naunyn. Arch. f. klin. Med., 1882.
——— Deutsche med. Wchnschr., Vereinsbeilage, iii, 1898.
Nelson's Loose-leaf Medicine, 1920.
Neumann. Syphilis, Nothnagel's Spec. Path. u. Therap., xxiii.
Pariser. Deutsche med. Wchnschr., xv, xvi, 1902.
Pawlow. The Work of the Digestive Glands, London, 1902.
Petri. Arch. f. Verdauungskr., xiv, 479, 1908.
Peyer. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xxii, 411.
Poly. Arch. f. Verdauungskr., xvi, 700, 1910.
Potter, N. B., and Wilson, T. C. Ortner's Internal Medicine, 5th ed.
Poulsson. Lehrb. d. Pharmakol., 1920.
Price, F. W. A Textbook of the Practice of Medicine, 1922.
Reichmann. Berl. klin. Wchnschr., xl, 1882.
——— Am. Journ. Med. Sc., April, 1904.
——— Ztschr. f. klin. Med., xiv.
Rheinbold. Arch. f. Verdauungskr., xiv, 34.
Ribbert, H. Lehrb. d. allg. Path. u. path. Anat., 1920.
Riegel. Ztschr. f. klin. Med., xxxvii, 387, 1899.
Rosenheim. Berl. klin., 1894.
Rosenow, E. C., and Sanford, A. H. The Bacteriology of Ulcer of the Stomach and Duodenum in Man, Journ. Infect. Dis., xvii, 219, 1915.
Rovsing. Samml. klin. Vortr., n. F., Aug., 1906.
Rutimeyer. Die geograp. Verbreit. u. Diag. des Ulcus Ventriculi Rotundi, Wiesbaden, 1906.
Sahli. Kor.-Bl. schweiz. Aerzte, 1902.
Sasaki. Arch. f. Verdauungskr., xii, 202.
Schiff. Arch. f. Verdauungskr., vi.

Schjerning. Handbuch der aerztlichen Erfahr. in Weltkriege, 1914-1918.
Schlesinger, E. Die Roentgen Diagnostik der Magen und Darmkrankheiten, 1917.
Schmidt, A. Deutsche med. Wchnschr., 1906, x, 435, 1911.
Schüle. Ztschr. f. klin. Med., xxix, 49, 1896.
Senator. Deutsche med. Wchnschr., vi, 1903.
Short, A. R. Index of Prognosis, and End-results of Treatment, 1922.
Sippy, B. W. Gastric and Duodenal Ulcer, Medical Cure by an Efficient Removal of Gastric Juice Corrosion, Journ. Am. Med. Ass., lxiv, 1623, 1915.
Skaller. Berl. klin. Wchnschr., 2189, 1909.
Spiro. München. med. Wchnschr., 1901.
Steele. Journ. Am. Med. Ass., Aug., 1906.
Stevens, A. A. Practice of Medicine, 1922.
Stiller. Arch. f. Verdauungskr., 1896.
——— Die æsthenische Konstitutionkrankheit, Stuttgart, 1907.
Strauss. Ztschr. f. klin. Med., xxix, 1896.
——— Diätbehandl. in Krankh.
Struempell, A. Spec. Path. u. Therap., 1920.
Tabora. Deutsche med. Wchnschr., vi, 242, 1911.
——— München. med. Wchnschr., lv., 1922, 1908.
Taylor, Alonzo. Osler's Modern Med., i, 277.
——— Practice of Medicine, 1922.
Tigerstedt, R. Lehrbuch d. Physiologie d. Menschen, 1919.
Trousseau. Clin. de l'Hôtel Dieu, Paris, iii, 1868.
Türck. Tr. Gastro-enterol. Ass., X Meeting, 1907.
Umber. Berl. klin. Wchnschr., iii, 1905.
Wagner. München. med. Wchnschr., 1904.
——— Arch. f. Verdauungskr., ii, 1905.
Weir. N. Y. Med. Journ., 1892.
Westerman. Centralbl. f. Chir., 356, 1910.

CHAPTER XXXI

DISEASES OF THE INTESTINES

HENRY WALD BETTMANN

ENTERITIS

ACUTE ENTERITIS

The treatment of acute enteritis is very simple. The indications are to empty the bowel, to give it rest, and to allay the irritation.

Nature has often emptied the bowel and removed the offending material before the advent of the physician. The presence of irritating substances is shown by the recurrence of crampy pains and by distention of the abdomen. A simple warm enema or a soapsuds enema is then useful in ridding the colon of gas, mucus, and food remnants. It is generally advisable to administer a purgative. If there is no nausea, castor oil is the best remedy. One tablespoonful or 2 may be taken plain, or mixed with whisky, sarsaparilla, or peppermint water. A hot-water bag applied to the abdomen is useful in allaying spasm. When nausea is present the castor oil will in all probability be vomited. Under these circumstances calomel is preferable. A single smart dose of from 3 to 5 gr. or more (0.2 to 0.3 gm.) is better than broken doses. For all but the mildest attacks the patient is better off in bed. In general terms we may say that all acute intestinal symptoms are an indication for bed rest. Rest for the intestine is obtained by abstinence from food or by a very simple diet. Hot tea containing a small quantity of milk and sugar is almost invariably well tolerated. Milk as a beverage should be avoided for the first few days. Boiled milk is often recommended for its constipating effect, but is always a treacherous food in acute bowel complaints. Clear bouillon is permissible, though not as reliable as hot tea. Toast or crackers may be taken with the tea. Browned flour soup has a deserved reputation for overcoming diarrhea. Cold drinks must be avoided. After the initial purgative has acted it is generally wise to give soothing or astringent drugs.

One-half a cup of hot water to which a teaspoonful of paregoric and a tablespoonful of brandy have been added with a little sugar is an exceedingly grateful remedy. This dose can be repeated in an hour and again in two hours, and is usually followed by sleep and relief from the symptoms. When pain is severe and the symptoms more urgent, the stronger preparations of opium may be used. Tincture of opium may be given in 10-drop doses every one to three hours until the bowels quiet down; or ¼ gr. (0.015 gm.) extract of opium combined with 10 gr. (0.6 gm.) of bismuth may be given every two to four hours until the desired result is obtained. Cohnheim advises the use of belladonna in preference to opium in the earlier stages.

It is usually advisable to push the remedies to their full constipating effect in order to avoid relapses. In the moderate cases more liberal feeding may be permitted from six to twelve hours after the cessation of the symptoms.

The albuminous foods are to be given preference during the following forty-eight hours. Soft-boiled or poached eggs, scraped beef, broiled steak, stewed or roasted chicken are all suitable. Toast, crackers, zwieback, and holland rusk may be eaten with impunity. Boiled rice or farina as well as macaroni and spaghetti are usually well tolerated. The vegetables must be added one by one. Boiled, baked, or mashed potatoes should be the first to be tried. Then follow asparagus tips and carefully prepared spinach. The patient must avoid the coarser vegetables and all fruits for four or five days after even moderate attacks, and for a week or ten days after the more severe ones. When the initial diarrhea has been intense it is frequently advisable to give some astringent for a week after the acute symptoms have subsided. The bismuth preparations are all useful in doses of 10 gr. (0.6 gm.) three to four times a day. The patient should not be dismissed from observation until the physician is assured that a return to the normal diet is not followed by a recurrence of symptoms. In this way relapses are avoided. This is especially important, as every attack leaves the bowels in a vulnerable condition and predisposes to later attacks. The treatment of the more violent attacks of acute enteritis often calls for nice judgment. When the stools are copious and watery, and when the patient is in a very prostrated condition, it often becomes necessary as a first consideration to check the diarrhea and stimulate the patient. A hypodermic injection of morphin, gr. ¼ (0.015 gm.), is indicated under these conditions; brandy or whisky may be freely used, preferably in the form of a hot toddy. Jamaica ginger is an agreeable addition, or the compound tincture of cardamom or other carminatives may be employed. Hot applications to the abdomen are always beneficial; it is not wise to use enemas under these circumstances except on the rare occasions when, notwithstanding the copious discharges, the bowel remains distended. The employment of drugs or chemicals in the wash water is

rarely of advantage, except when the lower end of the colon is affected (see Colitis and Proctitis).

After the initial prostration is overcome, there remains the original task of getting rid of the irritating material. Broken doses of calomel are now exceedingly useful, 1/10 to 1/12 gr. (0.006 to 0.005 gm.) being given hourly for ten successive hours. It is often of great advantage to combine minute doses of morphin with the calomel, giving gr. 1/24 (0.0025 gm.) every hour. Colon irrigations may now be ordered twice daily for two or three days.

The return to normal dieting must always be cautious after these severe attacks.

The fulminating attacks of acute gastro-enteritis, known under the names of cholera morbus and cholera nostras, yield to the treatment just described. Morphin is indispensable, and may be administered hypodermically or by mouth. Emetics are never needed, as the stomach is always emptied before the arrival of the physician. If a hypodermic syringe is not at hand, laudanum may be given in 10-drop doses every half hour, or an initial dose of morphin, gr. ¼ to ½ (0.015 to 0.03 gm.), may be placed dry on the tongue. If these remedies are vomited, they should be repeated immediately. If vomiting again follows, a starch enema containing 20 to 30 drops of laudanum should be employed, and this may be repeated every half hour for two or three doses if it is expelled. The physician must be on the lookout for signs of narcosis, and must grade the doses and the intervals between them accordingly. Brandy should be given if necessary. The patient must not be allowed much water. Cracked ice is permitted.

This treatment has come down to us from a former generation. Austin Flint says "that no apprehension need be entertained with respect to the sudden cessation of the vomiting and purging; the more quickly the arrest is made the better, after a free evacuation of the stomach and bowels. Mercury is, to say the least, superfluous. The success of treatment without it is all that could be desired."

The after treatment, after the control of the diarrhea, has been described above.

Certain peculiarities distinguish the acute diarrheas of old people. Free discharges are harder to control than in younger patients, and they lead more readily to fatal exhaustion. The use of opiates in the aged is also far more dangerous. For these reasons every acute diarrhea in an old person must be taken seriously. Reliance must be placed on hot applications, hot enemas, warm alcoholic stimulants, and astringent drugs, such as dermatol, tannigen, tannalbin, and bismuth subnitrate. Opiates are indispensable, but must be used with caution. Laudanum and the deodorized tincture of opium are to be preferred to morphin. Paregoric is an excellent remedy.

Dieting must be strict, but the total exclusion of food and drink is not warranted. Brown-flour soup, thick barley gruel, crackers with hot water poured over them may be allowed from the start. Rice cooked in milk, hot spiced claret, and hot tea are all useful and safe. Great care must be exercised in preventing relapses. The avoidance of chilled and all irritating foods must be insisted on for weeks following the attack.

Chronic Enteritis

(*Catarrh of the Small Intestine*)

Our knowledge of the pathological conditions affecting the small intestines is in a transition stage. In the past we have grouped under the one term "catarrh," or "enteritis," a number of different processes affecting different parts of the small bowel. The newer methods so ably developed by Schmidt and others are gradually bringing a clearer insight into the dark field. Already we are able to recognize certain intestinal disorders which are due to deficiencies of the gastric secretion (gastrogenic diarrhea) and of the pancreatic secretion (pancreogenetic diarrhea). The distinction between enteritis on the one hand and colitis on the other is more and more sharply defined, and treatment is becoming more rational and more direct in its application. At the same time we must not fail to recognize the fact that our knowledge concerning intestinal disorders is in a far from satisfactory state, that no really revolutionary facts have been established, and that our treatment of ten years ago remains for the greater part and with only minor variations the treatment of to-day.

The first step in the successful treatment of chronic enteritis is to discover, so far as possible, the etiological factors, and to remove them. Chronic enteritis is so often dependent upon venous congestion due to heart or kidney lesions, pulmonary emphysema, or hepatic congestion that a complete physical examination of the patient is called for in every case. The chemical examination of the gastric juice should never be omitted. The symptoms of enteritis are often the direct result of deficient gastric secretion, especially in cases of achylia gastrica, and many errors are made in the treatment of the symptoms by not recognizing the underlying cause. In achylia gastrica the amount of albuminous food must be greatly reduced; vegetable foods, on the other hand, are usually well tolerated. All foods must be finely subdivided; all coarse foods must be entirely avoided. The reader is referred to achylia gastrica for further details. In cases of gastric catarrh or marked hypochlorhydria the intestinal disturbance will never be successfully combated without attention to the primary condition; this is equally true of the other underlying conditions above named.

Following the lead of Cohnheim, we may divide the cases of essential intestinal catarrh into three clinical groups:

1. The mild cases without diarrhea, but with numerous symptoms, such as meteorism, abdominal pains, loss of strength, flatulence, etc.
2. The moderately severe cases with much intestinal fermentation and frequent attacks of diarrhea.
3. The severe cases with persistent diarrhea.

Certain hygienic measures must be adopted in all cases. The patient must take extra precautions against becoming chilled. He should use warm underclothing and socks, the usual abdominal flannel bandage being a useful addition. He must avoid exposure; the feet must not be allowed to be wetted in rainy or snowy weather; the baths should be of tepid water. Excitement of all kind must be avoided; business care and fret should be reduced to a minimum, and all violent exercise should be prohibited. For the aged and debilitated bed rest is a decided advantage, and this should be insisted upon whenever practicable in all acute exacerbations.

Mild Cases.—The mild cases require neither a very rigid diet nor any very active medical or mechanical treatment, but, as in all other cases of intestinal disease, *the treatment must be continued for many months.*

Three principles underlie the dietetic treatment:

1. The food must be especially well prepared, that is, soft, free from fibers and indigestible particles.
2. Coarse and irritating foods must be omitted.
3. Foods which easily ferment or putrefy must be prohibited.

Soft-boiled eggs are especially well adapted to this disease; the softer meats (sweetbreads, brains, boiled mutton, stewed chicken, whitefish, haddock) are equally useful. White bread, cornbread, whole wheat or Graham bread are all permissible. Various preparations of gelatin are well tolerated. Too much sugar must not be used. Cocoa and tea are the best beverages; white wines, beer, champagne, ginger ale are unsuitable, though a dry sherry or claret may be beneficial. Blackberry cordial has a deserved reputation when an astringent effect is needed. Only the soft vegetables should be taken, such as asparagus tips, spinach (chopped fine and passed through a colander), purée of potatoes or peas. If flatulence or meteorism is a marked symptom, starchy foods, such as cereals, cereal soups, and string beans or lima beans, must not be allowed. If these symptoms are not present the cereals are a valuable addition to the dietary. Farina, well-steamed rice, oatmeal prepared over night in a fireless cooker, spaghetti, and macaroni are all suitable. The coarser vegetables must under all circumstances be omitted. In this class we include cabbage, cauliflower, turnips, radishes, onions, tomatoes, horse-

radish, celery, celery root, oyster plant, etc. All fruits are objectionable. Sweets, such as honey, candy, preserves, jellies, marmalade, and sweet cakes, must be omitted.

The regulation of the bowels in the mild cases must be closely attended to. All strong purgatives must be strictly interdicted. In some cases a simple enema taken daily answers every purpose. As a matter of fact, the bowel movements in many cases are not particularly irregular. We must prevent our patients becoming addicted to the regular use of any laxatives, if possible. The salines dissolved in hot water and taken once or twice daily are preferable to other laxatives. Carlsbad salts in doses of 1 teaspoonful in a cup of hot water taken one-half hour before breakfast is suitable. Phosphate of sodium, sulphate of sodium, and sulphate of magnesium may be used in various mixtures combined with sodium chlorid or sodium bicarbonate. A trip to one of the well-known mineral springs, such as Harrowgate, Carlsbad, Kissingen, Vichy, Neuenahr, Wiesbaden, French Lick, Saratoga, Tate Springs, Tennessee, is often curative.

The use of the necessary reconstructive drugs, such as iron, arsenic, strychnin, quinin, should not be omitted in appropriate cases.

Moderate Cases.—The moderate cases of chronic enteritis are treated along the same lines as the mild cases, only the treatment must be more rigid and the use of drugs is a necessity. In addition to a study of the gastric digestion the physician must now attempt to determine the digestive activity of the intestines themselves. The test diet of Schmidt has been widely adopted and forms the basis of many similar dietetic tests which are designed to measure the digestive capacity of the bowels. The diet of Schmidt is given for three days or more. It consists of the following foods:

In the Morning.—0.5 liter milk (1 pint), 50.0 gm. of zwieback (1 2/3 oz. zwieback or rusk).

In the Forenoon.—0.5 liter of oatmeal gruel (made from 40.0 gm. oatmeal, 1 1/3 oz.); 10 gm. butter (1/3 oz.); 200 gm. milk (6 2/3 oz.); 300 gm. water (10 oz.); 1 egg.

At Noon.—125 gm. (4 oz.) chopped beef (raw weight), broiled rare, with 20.0 gm. (2/3 oz.) butter, so that the interior remains raw; to this 250 gm. (8 oz.) mashed potatoes are added.

In the Afternoon.—As in the morning.

In the Evening.—As in the forenoon.

After the third day the stools are systematically studied for mucus, the remains of connective tissue, meat fibers, undigested starch, fat drops, and fatty acid needles and soaps; also for parasites, ova, etc. Other tests determine the degree of carbohydrate digestion, the presence of bile pigment (bilirubin), and blood.

It is obvious that the findings after this test diet will largely deter-

mine what dietetic restrictions are necessary. Schmidt lays down several general laws.

Where there is marked intestinal fermentation the diet must be predominatingly albuminous. When the putrefactive changes are marked the diet should be composed largely of carbohydrates. In catarrhal conditions the food must be unirritating, easily digestible, and non-putrefying.

These three requirements, according to Schmidt, are best met by gruel soups, to which gradually a larger and larger quantity of milk is added. Milk has the minimum amount of putrefactive material, and is the one best food. When milk is found not to agree with patients, cocoa may be substituted. But Schmidt is unwilling to accept patients' statements that milk does not agree with them. By adding milk gradually to the other foods (cereals), a tolerance for it is usually established. When the milk actually produces fermentation the addition of salicylic acid overcomes this tendency. To the daily quantity (1.5 liters), 0.3 gm. (5 gr.) of salicylic acid is added in the following manner: the salicylic acid is stirred thoroughly in a little cold milk, then this is added to the daily portion, stirred well, and boiled once. The milk does not thereby lose its character or taste, nor does it coagulate.

Notwithstanding the conclusions of Schmidt, there is a rather widely accepted opinion that milk is a treacherous food in intestinal disturbances. When raw it is apt to cause flatulence, a sense of heaviness in the stomach, and frequently a coated tongue and a bad breath. Boiled milk is apt to be constipating, to form lumpy masses which lead to impaction of feces, and is very distasteful to many patients. As a rule, we can dispense with milk altogether, except as an addition to tea or gruels, and nourish the patient with a variety of the lighter foods enumerated before.

The medicines in the treatment of enteritis are selected chiefly from the list of sedatives and astringents.

Various preparations of opium are invaluable when there is much pain or a tendency to tenesmus. Opium must, however, be considered strictly an emergency drug to be given for definite indications and for a brief time. To continue the use of opium in the hope of "checking the bowels" over a long period is as unscientific as it is useless. Many patients afflicted with the milder forms of intestinal catarrh are made much worse by the long-continued use of opium, often self-administered in the form of paregoric or of some advertised nostrum. The various preparations of bismuth deservedly hold the front rank in the list of remedies. Subgallate of bismuth is especially valuable in doses of 0.5 to 1.0 gm. (7½ to 15 gr.) every three hours, or three times a day after meals. The subnitrate and the subcarbonate are equally useful; tannigen, tannalbin, bismutose, and numerous other preparations are highly efficient astringents. It must be borne in mind that the medicinal treatment is secon-

dary to the dietetic treatment, and that, when moderate doses of the above drugs are not effective in checking diarrhea, a change should be made in the diet and the doses of the drugs should not be inordinately increased. It is not an uncommon experience to see diarrhea progress unchecked while the patient is taking subnitrate of bismuth in teaspoonful doses every few hours. Some patients are even irritated and made worse by any insoluble astringents. Einhorn frequently prescribes the fluid extract of condurango and fluid extract of calumba, of each 20 drops (1.3 c.c.) three times daily.

The intestinal antiseptics are often useful. During acute exacerbations calomel in doses of gr. 1/10 to gr. 1/20 (0.006 to 0.003 gm.), repeated hourly, is often exceedingly useful, although calomel is no longer classified with the intestinal antiseptics, as it is known to increase the number of bacteria in the stools. Salicylate of bismuth, betanaphthol, creosote, and especially benzosol are of marked value. Cohneheim says that in cases in which the stools are persistently of a pulpy semisolid consistency with marked fermentation calcium salts combined with bismuth are most effective. He recommends the following prescription:

℞	Calcii carbonat.		
	Calcii phosphat.	āā ʒvi	25.0
	Bismuth. salicylat.	gr. lxxx	5.0

Sig. One teaspoonful three times daily after meals.

Cohnheim especially advises the physician not to jump from one remedy or one line of treatment to another with undue impatience, as the best lines of treatment are slow in their effects and must be persistently carried out.

Severe Cases.—The severe forms of intestinal catarrh constitute an obstinate affection, the successful treatment of which extends over many months or even years. The danger of relapses is ever present and the least indiscretions in diet or in the habits are apt to be followed by exacerbations. Bed rest is one of our most efficient means of combating the acute attacks and tiding the patient over into the full convalescence. Several weeks in bed is not too long a course, and this prolonged bed treatment will usually be rewarded by a long period of well-being, especially if combined with Priessnitz compresses, colonic irrigations, massage, and other hygienic measures. The dietetic rules have been outlined above. No other chronic complaint requires more skill and tact on the part of the physician, who must individualize his treatment to an unusual degree and know how to keep his patient in line under the many vicissitudes to which he may be subjected. A comprehensive and very valuable description of the methods which are used to prepare appropriate diets on a large scale for hospital patients will be found in the *Zeitschrift für physikalische und*

diätetische Therapie, 1911, Band xv. H. Strassner describes in detail the diet kitchen of Professor Schmidt in Halle, and gives many valuable dietetic suggestions and diet lists, worked out according to their indications and their caloric equivalents.

Enteritis in Infancy

No perfectly satisfactory classification of the diarrheas of infants has yet been made. Keeping as close as possible to the purely clinical point of view, we recognize diarrhea due to overfeeding, due to improper feeding, and the result of infectious processes. A class due to insufficient feeding also exists, but is comparatively uncommon. As is well known, infantile diarrhea is far more common in summer than at any other season, and predominatingly in bottle-fed children. This is due chiefly to the use of contaminated cows' milk and other substitutes for mothers' milk, but partly, also, to the heat itself, which reduces the infants' vitality and their powers of resistance. The prevention of summer diarrhea includes, therefore, several factors. The infants should be protected from the heat of, and especially the direct rays of, the sun; they should be very lightly clad; they should be frequently bathed, and should have cool drinking water offered them freely. Most important of all, the milk supply should be protected in every possible way, beginning at the dairy and ending with the care of the empty nursing bottles. Lastly, the special quantity of milk and its method of preparation must be specified for each individual child, according to its own requirements.

The treatment of the acute attacks, whether due to improper or excessive feeding, is based on very simple principles. The offending material must be expelled, and the bowel given rest. The old plan of administering an initial purgative has been much criticized of late as being often superfluous, and sometimes even harmful. Nevertheless, as a clinical procedure it has stood the test of time and is almost always beneficial. The two drugs most commonly used are castor oil and calomel. If the stomach is upset, calomel should be preferred. To an infant under six months, 1/10 gr. (0.006 gm.) may be administered hourly for five or six doses; to older children, the medicine should be continued until 1 gr. (0.06 gm.) has been taken. When the stomach will tolerate it, castor oil, in doses of 1 teaspoonful for the younger infants to 2 teaspoonfuls for the older ones, is an excellent remedy. In general terms, we may say that the presence of fever indicates the use of an initial purgative; in the absence of fever, the purgative, though usually useful, may often be dispensed with. When the bowels are distended with gas, or when there is straining at stool, or much mucus in the stools, a simple enema with physiological salt solution is of advantage. It is not ordinarily advisable, in the simple cases, to flush out the colon with large quantities of fluid, as much discomfort is often caused thereby. One pint is usually sufficient.

A certain number of hours of starvation are demanded in nearly all cases. When the stomach is filled with sour milk curds, lavage with a soft catheter to which a funnel has been attached is of immense benefit. In the non-infectious cases without fever, however, this practice can usually be dispensed with. The modern tendency is to limit the starvation period as much as possible. Prolonged starvation (thirty-six to forty-eight hours) often reduces the resistance of the child, and frequently causes the continuance of the diarrhea. It must not be forgotten, however, that in the large majority of cases the good effects of starvation far outweigh the disadvantages. No food at all is infinitely better than food which disagrees with the patient. Within the last few years the opinion of Finkelstein that sugar is the commonest cause of diarrhea in bottle-fed children has met with wide acceptance. Dennet has reported his results in a large series of cases of summer diarrhea treated without initial purgation or starvation, but merely by diluting the milk with water and omitting all sugar. He advises absolutely no preliminary treatment; the infants are placed at once on boiled milk and water *with no sugar added.* The younger infants receive one-third milk and two-thirds water, the older infants half and half. This is given every two hours in normal quantities. "In the vast majority of cases," says Dennet, "the stools become more solid within one or two days. When the sugar is added we should begin with small quantities, say ½ oz. (15.0 gm.) of sugar to the 24-hour amount of food, and gradually increase it up to 1 or 1½ oz. (30.0 to 45.0 gm.). Rarely does a baby who has had diarrhea stand more than that amount of sugar."

Those who cling to the older plan of initial purgation and starvation urge that the return to normal feeding be very gradual. It is better to avoid milk for the first few days. Nestlé's food is especially valuable at this stage. It should not be begun in too concentrated a form, 1 tablespoonful to 6 oz. of water making a good starter. If well tolerated it should be used to the exclusion of all other foods for several days, the return to milk being a gradual one. Cereal decoctions of various kinds are also invaluable. Strained barley or rice gruels, mutton broth thickened with rice and strained, are well borne. Albumin water, which is widely used, does not seem to me a suitable food, as it greatly heightens intestinal putrefaction. I have seen many bad results from its use. Boiled milk well diluted with barley gruel forms a good bridge over which to return to the normal milk feeding. Extreme vigilance must be exercised lest the return to milk be followed by a recrudescence of the symptoms.

Drugs are often necessary to control excessive peristalsis. Bismuth remains the favorite. The doses should be large. Ten gr. (0.6 gm.) of the subnitrate may be rubbed up in chalk mixture and should be given every two or three hours. Ladd strongly recommends the so-called "milk of bismuth" in 1 or 2-teaspoonful doses with each feeding. The various bismuth preparations have little or no advantage over the subnitrate.

Preparations of opium are sometimes indispensable. The one use to which they should be absolutely restricted is to *check excessive peristalsis, after the fever has subsided and all toxic material has been removed from the bowels.* The younger the infant the more caution must be exercised. The tincture of opium in 1 or 2-drop doses may be given every two to four hours. It should never be pushed to narcosis. Unsleeping vigilance is necessary to safety. Dover's powder, in doses of ¼ to ½ gr. (0.015 to 0.03 gm.), may be given every few hours to a child one year of age. The use of opium in young infants must always be considered dangerous. Occasionally it is a life-saving device, when the child is relaxed and watery stools seem otherwise uncontrollable.

Other drugs may be necessary to meet special indications. Brandy or whisky is useful in combating collapse. Fifteen to 30 drops may be given well diluted every two to four hours to infants from eight months to one year of age. Strychnin is occasionally needed. Doses of gr. 1/300 to 1/200 (0.0002 to 0.0003 gm.) may be given hypodermically every few hours. Tincture of strophanthus in ½-drop doses is often highly beneficial in strengthening the heart. Not much reliance can be placed on the old-fashioned aromatic infusions or teas for overcoming colic. Hot applications to the abdomen are useful; a catheter inserted into the rectum, small rectal injections, a few drops of paregoric or whisky in hot water, all are efficient when appropriately used.

Infants do not always respond well to the treatment outlined above. The bowels continue to be loose, the children are restless, and do not regain weight, the stools are offensive, irritating, and contain mucus or curds. In these cases Finkelstein strongly advocates his so-called Eiweiss milk (casein milk). It is prepared as follows, according to Dennet:

"One quart of milk is heated to 100° F. and 2 teaspoonsful of rennet or essence of pepsin added. This is allowed to stand from fifteen to twenty minutes until jellied, then heated to 150° F., constantly stirring. The whey is then drained off through a wire colander and thrown away. Enough cold water is added to make a pint in all. The curds and water are then pressed through the wire sieve or colander with a wooden spoon two or three times, until the curds become soft and fine. To this pint of curds and water one pint of real buttermilk (from the churn) is added. It should be used in the same amounts and at the same intervals as the boiled milk for a period of from three to seven days, or until the stools are hard and dry. Then the boiled milk and water are substituted for it and the sugar is gradually added to the food as above described. This feeding will rarely fail us in stopping the most resistant diarrhea. Finkelstein's theory of its action is that, the milk sugar being soluble in the whey which is discarded, the food is almost sugar-free."

The use of buttermilk in these subacute cases was first strongly advocated by a Dutch physician, Teixera de Mattos. According to Friedlander, it is prepared as follows: To a quart of fresh buttermilk 1 tablespoonful of wheat flour and 2 tablespoonsful of cane sugar are added; the mixture is then boiled over a slow fire under constant stirring. It should be allowed to boil up three times and is then to be strained. This forms the exclusive diet of the infant for days, and is almost always followed by most gratifying results.

INFECTIOUS DIARRHEAS AND CHOLERA INFANTUM

The effort to classify the acute intestinal infections according to the infecting organism (Shiga bacillus, colon bacillus, gas bacillus, Bacillus pyocyaneus, *et al.*) has not as yet led to practical results which can be applied therapeutically. In fact, the difficulties of classification are as yet insurmountable. The persistence of fever is supposed to distinguish the infectious diarrheas from attacks of simple intestinal indigestion. At the present state of our knowledge it is wiser to neglect the bacteria and to treat the child. The treatment of the milder forms of infectious diarrhea has been outlined above. Cholera infantum is becoming a rare disease in this "century of prophylaxis."

Cholera infantum is characterized by continuous vomiting and purging, rapidly leading to collapse. The babies are comatose, have cold skin, subnormal temperature, incontinence of feces, and pronounced ischuria or anuresis. The very severe cases are apt to prove fatal under any treatment. Energetic means are necessary if the baby is to be saved. The hot mustard bath is a valuable stimulant; a tablespoonful of mustard should be used in each gallon of water. The baby should be wrapped in warmed flannels. Morphin is an invaluable though dangerous remedy. A child one year old may have gr. 1/50 to 1/100 (0.0012 to 0.0006 gm.) combined with atropin sulphate, gr. 1/500 to 1/800 (0.00012 to 0.000075 gm.), hypodermically, and this may be repeated in one hour and then at greater intervals. Hypodermoclysis is frequently of great help in warding off a crisis due to the loss of fluids and the inability to swallow any. Four to 8 oz. (120.0 to 250.0 c.c.) of physiological salt solution may be administered every four to six hours under the most rigid aseptic precautions. Even smaller quantities (1 to 2 oz., 30 to 60 c.c.) may have to be given at first, and more frequently repeated. Caffein is a most valuable stimulant. The sodiobenzoate may be given hypodermically in doses of gr. ¼ to ½ (0.015 to 0.03 gm.). Camphor may help sustain the heart. External heat is necessary.

Should the child survive the early collapse there is hope of saving it,

but extreme vigilance and attention to details are necessary. The nourishment at first may have to be limited to sips of warm water. Very thin strained barley water is the safest food to begin with. In some instances ice-cold milk is advisable; it is sometimes retained when all warm liquids are rejected. The buttermilk mixture described above may be given ice cold. The eyes should be protected during the stage of collapse by means of boric acid compresses. The mouth must be frequently but gently washed out with a warm borax or soda solution. Even apparently hopeless cases may occasionally be saved by sudden change of climate. Removal to Michigan, or, better, to the sea may have most astonishing results during excessively hot weather.

COLITIS

It is customary to consider the inflammations of the small and large intestines together under the designation "enterocolitis." This is entirely proper for these conditions as they occur in childhood, for at this period of life the two parts of the intestinal canal are usually affected together, although in different degrees. But in adults the matter is entirely different. A mild degree of colitis nearly, if not quite, always accompanies the acute and chronic inflammations of the small intestine, but the reverse is far from true. Not only do various forms of colitis occur as independent affections, but our therapeutic efforts gain enormously in directness and efficiency when we recognize the fact that we are dealing with five feet of intestine instead of twenty-five, and that the diseased tissues are readily accessible to medication from below.

The treatment of that form of colitis which accompanies acute enteritis has already been considered. Washing out the colon with physiological salt solution (roughly, 1 teaspoonful to each liter of warm water) has a most soothing influence. This may be repeated once or twice every twenty-four hours. Other solutions are also suitable, such as 1 teaspoonful of tannic acid in 2 quarts of water; weak solutions of boric acid; 5 to 10 per cent aqueous solution of fluid extract of krameria; weak infusions of chamomile tea. If there is much straining or tenesmus, rectal suppositories containing opium and belladonna are useful. An injection of weak starch solution containing 20 drops of tincture of opium is an old and approved remedy to allay irritation of the lower end of the bowel.

Chronic Mucous Colitis

Nothing in medical literature is more confusing than the conflicting descriptions of those diseases of the colon which are characterized by the discharge of mucus. There is a rapidly growing tendency to recognize a

catarrhal process as the underlying basis in all cases and to ascribe the protean character of the clinical course to various complicating pathological conditions, such as neurasthenia and hysteria, adhesions (pericolitis), appendicitis, bacterial infections, visceroptosis, etc.

The clinical history of mucous colitis runs the gamut from the simplest abdominal distress with slight mucous discharges on the one hand to the severest attacks of mucous colic, or "myxoneurosis intestinalis" on the other. Between these two extremes we encounter all degrees of discomfort, pain, nervous debility, and constipation or diarrhea in confusing association.

I think that we shall profit greatly in our treatment of these cases if we divide them into two groups:

Group 1 presents the combination of pain along the colon and a tendency to diarrheal discharges.

Group 2 occurs in nervous individuals who suffer from chronic constipation and who have periodic attacks of "membranous colitis" or "mucous colic." This distinction, while clinically useful, cannot always be made with certainty. We must also clearly recognize the fact that a proportion of these patients cannot be cured by medical means alone, but that the symptoms are kept up indefinitely by adhesions, appendicitis, or other conditions which can be removed only by surgical procedures.

Cases of Colitis with Colonic Tenderness and Diarrhea.—The principle underlying the treatment of these cases is to spare the bowels from irritation from above and to apply soothing remedies from below. The proper diet is the one already described as suitable for cases of chronic enteritis. Albuminous foods (meat, eggs) must predominate; the coarser vegetables and fruits must be altogether excluded. The reader is referred to the article on enteritis for further details. Drugs by the month play an important rôle. The various preparations of bismuth are the most generally useful; benzosol in 5-gr. (0.3 gm.) capsules, ichthyol in 3-gr. (0.2 gm.) pills, and other intestinal antiseptics and astringents are helpful. We should avoid constipating our patients; on the other hand, purgative medicines all do harm, with the possible exception of castor oil. Castor oil can often be administered with great benefit in tablespoonful doses on alternate nights, or daily before breakfast (method of Hale White), for a period of two or more weeks. The use of salines, even in small doses, or in the form of medicinal spring waters, is not to be countenanced. An occasional dose of Epsom salts may be necessary in some cases.

An important factor in the treatment is the use of proper enemata. X-ray examinations have clearly shown that small quantities of fluid administered with the patient in the knee-chest position readily find their way along the whole colon into the cecum. The nozzle of the syringe need not be introduced further than just within the sphincter. The use

of large or long so-called colon tubes is becoming obsolete, as it is now well known that these tubes rarely, if ever, pass beyond the rectum. The fluids should be slightly above the body temperature. The quantity need rarely exceed 1 liter; in fact, ½ liter (1 pint) is usually as efficient as larger quantities. To distend the bowel with large quantities of fluid (2 or more liters) has no obvious advantage and many disadvantages, as it often seriously disturbs the patient's comfort, and in some cases keeps up the irritation or inflammation. Nitrate of silver is an excellent remedy. To avoid causing pain 1 pint of a 1:10,000 aqueous solution should be used the first night before the patient retires; the strength may be rapidly increased to the point of tolerance (burning pain), which will usually be reached when the solutions have a strength of 1:1,000 or 1:2,000.

Recently it has become customary to irrigate the colon with huge quantities of hot water with or without medicaments. A two-way irrigator is essential. As much as 4 or 5 gallons of fluid may be employed once or twice daily. The patient may be in the knee-chest position or, better, in the left lateral with raised buttocks. Sodium bicarbonate, tannic acid, argyrol or other drugs may be used. Hot water at a temperature of 120° F. has been recommended by Logan. The irrigation may require from twenty to thirty minutes' time and should be continued until the water returns clear.

Similar results are aimed at by the so-called transduodenal lavage. A duodenal bucket is introduced. When it is in place about 1 liter of hot water containing 0.9 per cent each of sodium sulphate and sodium chlorid is slowly instilled. Purging may begin in about one-half hour and may continue for an hour or two.

Schmidt in Germany and Gross in this country advise the insufflation of oxygen through the duodenal tube, but the method has not been extensively used and probably has no specific value.

Within the past few years efforts have been made in the direction of making vaccines from the various groups of intestinal bacteria. This method of treatment has not as yet demonstrated its value sufficiently to warrant wider adoption.

Mummery recommends 0.5 per cent solution of protargol or argyrol. Other useful injections are salicylic acid, 1:1,000, and tannic acid, 1:200. The injections should be given daily at first, then on alternate days, and should be kept up until mucus no longer appears in the stools. The chronic nature of this ailment and its tendency to relapse should be remembered and the vigilance of the physician should not be too early relaxed.

Constitutional treatment will be required in most cases, as the majority of patients belong to the neurotic class. Iron, arsenic bromids, and other tonics or sedatives must be administered according to indications. One

warning is in order: Many patients form the habit of inspecting their stools and keeping sharp lookout for food remnants, mucus, or other abnormalities. They develop a characteristic type of hypochondriasis, which must be actively combated. In such cases it is best to omit all local treatment in order to divert the patient's mind from the local condition, and it is often necessary to allow an unlimited diet, paying no attention to the intestinal discomfort until the general health of the patient is properly built up.

Treatment of Membranous Enteritis or Mucous Colic.—Membranous enteritis is now recognized as a form of catarrh of the colon associated with constipation. The so-called mucous colic is an acute exacerbation in the course of membranous enteritis, often due to nervous influences, but frequently dependent upon anatomical or inflammatory complications. Nothnagel's theory of the purely nervous origin of mucous colic must be dropped. A postmortem examination or an operation will reveal some abnormality in nearly all cases. In 66 cases reported by Mummery, in which a definite lesion was found, the following conditions were present: adhesions causing kinking or obstruction, 14; coloptosis, 5; chronic appendicitis, 5; inflammation or displacement of the uterus or appendages, 2; previous operation on the colon, 2; chronic inflammation of the colon, 30; cancer, 7; fibrous stricture of the sigmoid, 1. We thus observe that in nearly or quite one-half of all cases some surgical measures will have to be employed if a permanent cure is to be effected. In the other half a cure can be brought about by purely medical and dietetic methods.

The treatment during the attack is purely symptomatic. If the pain is intense the patient must remain in bed until the "membranes" are discharged. Hot applications to the abdomen are useful. Hypodermics of morphin may be required. Belladonna may be given internally, or, better, atropin may be given hypodermically with the morphin. The bowels should be thoroughly washed out. Very warm salt solution is the best fluid to inject, although a pint of warm olive oil is often effective in relieving the pain. The olive oil enema must be followed in an hour or more by a salt water injection. This may have to be repeated, and sedatives may be required for from twenty-four to thirty-six hours.

After the attack is over the patient is treated dietetically and by injections into the bowel.

To von Noorden belongs the credit of pointing out the correct principles for the dietetic treatment of these cases. He recognized the rôle that constipation played in the symptomatology, also the necessity of keeping the colon full instead of empty, and the further necessity of nourishing the patient as fully as possible. Von Noorden ordered a diet very rich in cellulose, copious in quantity, and more or less indigestible in quality. Coarse bread should be taken in liberal amount; the cruder vegetables, such as cabbage, celery, tomatoes, radishes, turnips, carrots, are to be

eaten freely; fruits must be consumed in quantity; the smaller fruits, such as berries, currants, grapes, are to be preferred. Bran in 1 or 2 tablespoonful doses may be taken once or twice daily. Sweets must be avoided, also too much starchy food, tea, cocoa, coffee, and alcoholic beverages. Fats are a necessary part of the régime. Their general utility in nervous patients is now well recognized. They also help to make the feces soft and copious. Butter must be taken as freely as possible; cream is a useful adjunct. The fatty meats, such as pork and bacon, are valuable. Care must be taken not to overload the patient's stomach with fat, and thus interfere with the digestion. Olive oil may be taken inwardly, also liquid petroleum and albolene.

The advantages of the von Noorden diet promptly show themselves. The bowels soon begin to act spontaneously, the patient gains in weight and strength, the nervous symptoms grow less. Sometimes, however, the sudden change to the von Noorden diet brings a series of new symptoms in its train. The intestines are not able to cope with the coarse foods; the patient feels bloated, uncomfortable, and may have a regular "bilious attack." After a few days the bowels may "rise to the occasion" and take up their functions more adequately. To tide the patient over the first week or two it is often advisable to keep him in bed, to apply Priessnitz compresses to the abdomen, and to order mild abdominal massage daily. Einhorn overcomes the difficulties of the von Noorden method by making the transition from the sparse to the robust diet a gradual instead of a sudden one. He does not consider the indigestible residue an essential part of the treatment, but insists merely that the patient be slowly trained to take the foods of an ordinary healthy individual. The goal sought is a good state of nutrition, and, therefore, meat, eggs, and cereals should be taken freely. The coarser foods should be added only so fast as the digestive capacity of the individual will permit.

My own experience has led me to cling to the von Noorden method. A suitable diet to begin with will be described later in the section on Constipation. This diet rarely disagrees with the patient, very seldom causes marked symptoms of indigestion, does not require bed rest or local applications, and is usually followed at once by normal fecal evacuations.

Fleiner introduced the use of systematic oil injections in the treatment of this disorder, and they have been universally adopted as the best remedial agent we possess. The injections are given every night for three weeks, then every other night for three weeks; from the sixth to the tenth week they should be given twice a week, and may be continued at longer intervals for several months more. Olive oil should be employed. Cheaper oils, such as sesame and cotton-seed oil, have been recommended, but they are more irritating than pure olive oil. About 8 oz. (250 c.c.) of olive oil, warmed to the body temperature, should be introduced at bedtime with the patient in the knee-chest position, and the

patient instructed to retain the oil overnight. In some patients there will be a disagreeable leakage of oil during the night, and the bed linen will be soiled. This may sometimes be avoided by raising the buttocks of the patient for one-half to one hour after the injection, but this is not always effective, and a rubber sheet may be found useful in protecting the bed. By reducing the quantity of oil to 4 oz. or even less (120 c.c.) this leaking may usually be avoided; the quantity should then be increased gradually until the full quantity, 8 to 16 oz. (250 to 500 c.c.), is taken nightly. Eight oz. (250 c.c.) usually answers every requirement, and there is rarely any advantage in using the larger quantities.

Upon awaking in the morning the patient should try to evacuate his bowels and should make the effort at the same hour daily. Occasionally salt enemata will be required during the first few days, but if the above-mentioned dietetic rules are carried out the enemata can usually be dispensed with. Nearly all patients will benefit by constitutional treatment. Iron, arsenic, the bromids, and other remedies, such as strychnin and quinin, will be required as indicated. General massage and hydrotherapeutic measures can often be employed to advantage. Castor oil may sometimes be necessary at the outset of the treatment. Wylie has recommended a 1-oz. (32 c.c.) mixture of castor oil and glycerin three times daily for several weeks to produce soft, copious stools. While the chief object of the treatment is to overcome the constipation by natural means and bring about daily evacuations without drugs, Wylie's mixture will be found very useful in some obstinate cases.

When medical measures fail to bring the necessary relief, surgical interference should be considered. The severity of the symptoms will usually be the deciding point in regard to the advisability of surgery. When the symptoms are only moderate the neurotic state which most of the patients present would weigh against the expediency of an operation. In the presence of severe and health-destroying symptoms, however, an operation should be undertaken. An exploratory laparotomy should be made, the necessary adhesions severed, and the appendix removed if diseased. Right-sided colostomy has been performed for this condition, also ileosigmoidostomy. The former is open to the objection that the patient is worse off with his artificial anus than he was with the colitis; the latter is too serious an operation for the disease in question. Appendicostomy or cecostomy would seem to be the operation of choice when the only lesion found is a catarrhal colitis. Mummery has collected 20 cases; 13 of the patients were permanently cured. As abdominal surgery progresses, probably other operations will be found useful for this condition.

Ulcerative Colitis

The general use of the sigmoidoscope has revealed the fact that various mild degrees of ulceration of the colon are by no means uncommon.

Formerly only the more serious forms of ulceration were recognized, and ulceration of the colon, except when due to chronic dystentery, was considered a practically hopeless disease. Chronic catarrhal and chronic follicular ulcer are usually amenable to medical treatment, and can be entirely cured in the majority of cases. The treatment does not differ essentially from that already described as applicable to cases of chronic catarrhal colitis. Irrigations of the colon play a more important rôle, and more attention must be paid to the general care of the patient. Sea air, cold baths, general tonic medication, are all important. The diet at first should be strictly limited (see diet for Chronic Enteritis), but far greater liberty should be permitted as soon as the ulcers take on a healthy appearance. Bed rest is desirable early in the treatment; hot Priessnitz compresses are useful in relieving the pain and in stimulating the healing.

The colon irrigations may be performed twice daily in the beginning of the treatment and once daily after the first week. I have had most favorable results with injections of tannic acid (1:200) and nitrate of silver, 1:10,000 to 1:1,000. Other authors advise fluid extract of hamamelis or hydrastis, 2 to 5 per cent; fluid extract of krameria well diluted, boric acid, 1:100, and other antiseptics. Instead of the old-fashioned injections which the patient is instructed to retain as long as possible, colon irrigations with a tube and funnel have gained in popularity. The patient takes the knee-chest posture; the tube is introduced just within the anus, and the irrigating fluid is allowed to run into the bowel and out until it returns clear. Various irrigating devices and instruments have been invented. The water should never be cold, and the weaker solutions should be given preference at first, the strength being gradually increased as the tolerance of the patient permits.

For ulcerative processes of the lower bowel Soper strongly recommends the insufflation of calomel through the sigmoidoscope. To prevent corrosion of the tube the calomel should be mixed with an equal quantity of bismuth subcarbonate. As much as 2 or 3 drams of calomel (8.0 to 12.0 gm.) may be used at one sitting. The patient is placed in the knee-chest position. The ordinary sigmoidoscope is employed. Through a de Vilbiss powder insufflator with an especially long tube the calomel mixture is blown as the sigmoidoscope is slowly withdrawn. A pledget of cotton is held over the open end of the tube. These treatments should be administered daily and may be continued for weeks if necessary. The calomel has a purely local effect; no constitutional symptoms have ever been observed.

Internal remedies will frequently be useful. Small doses of opium are invaluable early in the treatment to allay the pain and the irritability of the bowels. Care must be taken not to constipate the patient. The concomitant use of opium and castor oil is to be recommended. Opium may be given during the day and the castor oil at bedtime. The various

preparations of bismuth are of little value. Tonics and stomachics will be needed during the first few weeks of treatment.

The severer forms of ulcerative colitis are due to many causes, which are only partly understood. Many cases run a rapid course with uncontrollable diarrhea, progressive emaciation, and exhaustion. Some ulcers perforate, leading to fatal peritonitis. The chief symptoms are pain, diarrhea, and the appearance of pus and blood in the stools. The sigmoidoscope reveals the presence of ulcers in the sigmoid and upper part of the rectum. A rare form is the hemorrhagic colitis, which is usually acute in onset and accompanied by profuse hemorrhages, which rapidly exhaust the vitality of the patient. The tuberculous and dysenteric ulcerations will be considered elsewhere.

The treatment of all forms of ulcerative colitis should at first be medical and on lines already described. The hemorrhagic form, which is exceedingly rare, must be actively combated; the patient should be absolutely starved for forty-eight hours; very hot colon irrigations with salt solution or tannic acid should be tried; tincture of opium should be given in large doses (20 to 30 drops); morphin may be necessary hypodermically; ice-bags and cold applications do no good and should not be tried. Mummery strongly urges that no time be lost with palliative measures; that an immediate appendicostomy be performed, and that the colon be irrigated through the appendix with a 1 per cent solution of argyrol or hazelin until the bleeding stops. The irrigations should be repeated every three to four hours. Zweig advises the internal use of fluid extract of hydrastis in doses of 20 to 30 drops, or of the fluid extract of hamamelis, ½ to 1 teaspoonful several times daily. In life-threatening hemorrhages he also recommends the subcutaneous use of gelatin. Gelatin may be given internally according to either of the following formulæ:

℞	Gelatini	℥iss	45.0
	Eleosacchari citri	ʒxi	40.0
	Suprarenin (1:1,000 sol.)	gtt. lxxx	
	Aq. dest.	℥xvss	450.0

M. Sig. One tablespoonful every three hours (Cohnheim).

℞	Decoct. gelatin alb. puris	15.0-200.0	ʒiv-℥vii
	Eleosacchari citri	50.0 c.c.	ʒxii

M. Sig. One or 2 tablespoonsful every hour (Zweig).

Transfusion of blood is indicated and is far more likely to save the patient than other methods.

When medical treatment is not producing good results and the patient is losing ground, recourse may be had to operative treatment. The only operations which are now performed for ulcerative colitis are cecostomy

and appendicostomy. Both operations have produced good results in certain cases.

APPENDICITIS

The pathologists describe many forms of appendicitis. The clinician may content himself with the simple classification into two varieties—the acute and the chronic. He may, if he chooses, subdivide the acute into two classes, the apparently mild and the apparently severe. The chronic cases fall into three divisions—the recurrent, the relapsing, and the residual.

Acute Appendicitis

Acute appendicitis is a surgical disease, that is, an operation should be resorted to as soon as the diagnosis is certain. This conclusion is justified by the following observations: the disease is very treacherous; in any given case it is not possible to estimate accurately the severity of the attack; the immediate operation has an almost negligible mortality; complications which endanger life or might render the convalescence tedious are avoided; the operation usually results in a restoration to perfect health.

Medical treatment, on the other hand, is uncertain in its results; dangerous or fatal complications may arise unexpectedly; even if the patient recovers he is left with a damaged appendix and is very likely to have further attacks. If an abscess is allowed to form, the disease, even after an operation is performed, is protracted for many weeks and leaves the patient with a weakened abdominal wall.

No one thinks now of treating a case of acute appendicitis medically if surgical aid can be obtained. Even in the smaller and more sparsely settled communities a properly trained surgeon can usually be reached within from twelve to twenty-four hours after the onset of the symptoms. Granting these truths as now indisputably established we must not therefore entirely lose our perspective of the facts. We must not forget that the great majority of mild or even moderate cases will recover under competent and watchful medical care. We also should not close our eyes to the fact that uncritical haste to operate leads to the performance annually in America of hundreds of uncalled-for appendectomies.

Medical Treatment of a Mild Attack.—We are justified in making a diagnosis of acute appendicitis when the patient has pain, fever, local tenderness, and muscular rigidity. In addition there may be vomiting and other gastric symptoms. Constipation is almost invariably present. The severity of the attack is measured by the intensity and persistence of the pain, the general condition of the patient, and the pulse rate. The

temperature is a poor guide, and the degree of leukocytosis is sometimes misleading.

The one absolute indication in every case is perfect physical rest in bed. The dorsal position with the head slightly raised is the favorite one. If the initial pain is severe a hypodermic injection of morphin is indicated. One-sixth or ¼ gr. (0.01 to 0.015 gm.) may be given at once and repeated in a few hours if required. After the initial hypodermic injection it is usually advisable to continue the narcotic treatment, if such is needed, by moderate doses administered by mouth. The one principle to follow is to take the edge off the patient's suffering without narcotizing him.

The exact dose which will accomplish this result is the exact dose to give. The surgeons are right in demanding that the symptoms be not masked by overdosing with morphin. On the other hand, the patient demands relief and is entitled to the maximum relief which can be given within the bounds of prudence. The careful use of morphin masks nothing, lessens the shock, quiets peristalsis, reduces the tendency to vomit, and is indicated in almost every case. To withhold it on theoretic grounds is not good medicine. While internists agree on the necessity for opium in the early stage, there is some diversity of opinion regarding the best method of administering it.

Personally I favor an initial hypodermic of morphin, gr. ⅙ to ¼ (0.01 to 0.015), followed by a solution of morphin containing gr. 1/12 (0.005 gm.) in each teaspoonful, 1 teaspoonful to be given by mouth every one to three hours if required. Einhorn strongly recommends Sahli's method of giving 10 to 15 drops of tincture of opium every hour until the pain materially subsides, then 5 or 6 drops every two or three hours until the pains are gone. They prefer opium to morphin on the ground that it allays peristalsis more completely.

Forchheimer advises minimal doses of morphin or opium and calls attention to the fact that minute doses are often sufficient to reduce the pain. As a general rule, small doses suffice to quiet the patient in mild cases without early peritoneal involvement. The patient must lie absolutely quiet. Turning in bed is strictly prohibited. The bed-pan or bed urinal must be used for evacuations. The legs may be held in any position comfortable to the patient. If he is more at ease with the knees flexed, pillows may be advantageously used to keep them in the desired position.

Nearly all clinicians agree upon the advisability of absolute abstinence from food during the first twenty-four hours. Ice pellets may usually be permitted. Gastric lavage is rarely indicated. There is little justification for its routine use. Nature usually promptly empties the stomach when the attack begins within a few hours after a meal. Gastric sedatives, with the exception of morphin, are out of place, and morphin

should not be used until the stomach contents are completely evacuated and then with caution.

An ice-bag should be applied immediately to the right iliac region. The ice-bag reduces local congestion and inflammation; it lessens the pain and tends to reduce the pulse rate. It also antagonizes shock. If there is much distention two ice-bags may be used, one on each side of the median line covering the lower half of the abdomen.

The bowels must be let severely alone. This principle, I believe, is now universally adopted. What the patient needs is absolute rest and the absolute cessation of intestinal peristalsis. To move the bowels is to invite trouble. Neither low nor high enemas are in order. An ineffectual enema is often taken by the patient before the arrival of the physician. The absence of any relief by the enema is in fact a good diagnostic feature of appendicitis. The first twenty-four hours' treatment is, therefore, clearly mapped out. It may be thus summarized: enough morphin to control pain, absolute physical rest in the dorsal position, an ice-bag over the right iliac region, starvation, and the avoidance of laxatives and enemata.

In mild cases the patient will be reasonably comfortable on the second day. Fever will be moderate, the pulse rate will be under 90, regular, and of good quality, and the need for narcotics will be either greatly diminished or altogether gone. There will still be tenderness at McBurney's point and some rigidity of the muscles on the right side of the abdomen. The chief duty of the physician at this stage is to be cautious. The treacherous nature of appendicitis is in part due to lack of vigilance on the part of the medical attendant. While it is true that perforation and diffuse peritonitis may occur insidiously and progress while the patient seems to be doing well, nevertheless, this course of the disease under the watchful care of an experienced clinician must be considered decidedly exceptional. A good pulse rate, the absence of general abdominal distention, the patient's mental and physical comfort, a desire for food, must all be considered favorable signs and indicate that the inflammation is receding. So long, however, as local tenderness persists, and so long as even the least muscular rigidity remains on the right side, the utmost caution is in place. Liquid food may be given in favorable cases on the second day. Only small quantities must be taken at a time. Broths, tea, and toast should be preferred to milk or cereals. Milk is an unreliable food in all intestinal conditions. On the third day cereals may be taken; ice cream is often well tolerated, especially in children. A light, easily, digested diet may gradually be resumed after the fifth day if the symptoms and signs have all disappeared. So long as pain or muscular rigidity remains absolute quiet must be insisted on. Many fatalities have been due to the violation of this rule. To try to hasten recovery is to create danger.

The bowels may be moved by a low enema on the third or fourth day, depending on the progress of the case. Sometimes it is advisable to give a preliminary injection of 4 or 6 oz. of olive oil. The nurse must exercise due caution in giving the enema; the patient is to move as little as possible, and under all circumstances must avoid straining; naturally a bedpan must be used.

A successful enema which produces no pain or special discomfort may be taken as a good sign, and the enema should be repeated daily thereafter until the patient leaves his bed. Should the enema produce much distress or markedly increase the pulse rate, or should the patient experience great difficulty in expelling the water, there is need of increased caution on the part of the physician. Every patient who is doing well should improve without interruption. Exacerbations of pain or of bloating are danger signals. The ice-bag may be removed when the fever has been absent twenty-four hours and when the local signs have disappeared. In the mildest cases convalescence should be fully established between the seventh and the tenth day, when the patient may leave his bed part of each day and increase his diet. The physician must explain to the patient the probability of a relapse or a recurrence. Precautions must be taken for from six months to a year after the attack. The patient must avoid all gymnastic or athletic exercises; he must regulate his bowels, with laxatives if necessary. He must avoid coarse vegetables and raw fruits, and must be careful not to "spoil his stomach." He should report the least pain in the abdomen to his physician. Many patients prefer to undergo a "preventive appendectomy" rather than to submit to the doubtful prophylactic measures just outlined, and the best practice is in accord with this decision. A patient who has had an attack of appendicitis is liable to have others, and it is safer for him to undergo an "interval operation" at the hands of an expert surgeon than to take his chances with a new attack. Some patients, however, refuse the operation after the first attack. A certain proportion of these remain well; others suffer from recurrences. Some attain good health after numerous attacks, the appendix finally becoming quiescent, but this is the exception rather than the rule. Frequently adhesions form about the appendix, the patient becomes the "residual legatee," and suffers from various chronic symptoms on the part of the digestive system without ever having new frank attacks.

All of these facts should be laid before the patient. Patients who lead guarded lives and remain constantly within the reach of surgical assistance run less risk in postponing an operation. Those who travel much or live in secluded sections take a correspondingly larger risk in retaining their appendices.

In cases which have been so mild that some doubt is felt regarding the diagnosis the physician is warranted in advising against an operation.

In all other cases, however, he should throw the weight of his authority on the side of a prophylactic appendectomy.

The surgeons are not yet of one opinion regarding the time which should be allowed to elapse after an attack before the "interval operation" should be performed. After a fairly smart attack it seems wiser to wait at least several weeks until any still active virulent bacteria in the neighborhood of the appendix may have either died out or at least have lost their virulence.

Treatment of Severe Attacks of Appendicitis.—Immediate operation is indicated in all severe attacks. But immediate operation by an experienced surgeon is not always practicable, and, while it is highly desirable, it is not always a necessity. Internal treatment may be decidedly preferable to an operation by an inexperienced surgeon. Finally, proper early medical treatment is of enormous importance in safeguarding the life of the patient until an operation can be performed.

The severity of an attack is usually revealed by the intensity and persistence of the initial pain, the degree of shock, the rapidity and quality of the pulse, the facial expression of the patient, and the amount of muscular rigidity. The temperature is a useful but a deceptive indicator. Early peritoneal involvement is characterized by intense muscular rigidity, severe pain, rapid pulse, and an expression of anxiety.

As in the milder attacks, the first indication is to administer a sufficient dose of morphin to relieve the pain and shock. One-quarter gr. (0.015 gm.) may be given hypodermically, and may be repeated in a short time. The attending physician must not be deterred by the fear of masking the symptoms.

Yates pithily asks of what good to the patient are symptoms after the alarm has been sounded and the diagnosis made?

The patient must be starved for at least twenty-four hours. Ice pellets may be permitted in some cases, but the patient must swallow little fluid. The best position is the dorsal. The thighs may be flexed on the abdomen if the patient wishes it. A semireclining posture, or the so-called Fowler's position, is not ordinarily an advantage. Where shock is severe it may be even contra-indicated, and the patient does better with the head and chest low. Hot bottles to the extremities are useful. An ice-bag over the right iliac quadrant should be maintained in position from the start. A second ice-bag on the other side is sometimes required. Some clinicians still advise a small low enema carefully given to empty the lower bowel. On the whole, it is safe to omit the enema for fear of starting undesirable peristalsis.

With the patient thus launched on his perilous journey, the further treatment will depend entirely on circumstances. If good surgical intervention is available, it is always better to operate than to await results. Formerly surgeons did not like to operate after the second day, if the

patient could be safely tided over to the interval. The factor of safety, however, is so hard to determine that the tendency is more and more to operate as soon as the diagnosis is made, no matter what the stage. Kelly thinks that no hard and fast rule can be laid down. Halsted says:

"If a case is on the rise, operate! if it is on the fall, you may wait; if a case is falling, but not fast enough, one is prone to operate to relieve anxiety."

Kelly divides the cases seen after the second day into three groups:

1. Cases which are manifestly getting worse, as shown by quickening pulse, rise of temperature, increase of swelling, pain, and tenderness.
2. Cases in which the patient, though not growing worse, is not distinctly improving, and there is a suspicion of latent trouble. Classes 1 and 2 should be operated on without delay.
3. Cases which are undoubtedly on the mend.

This group causes the consulting surgeon serious anxiety, and the decision to operate will often be determined by external conditions, such as the distance of the patient from "emergency help," the judgment of the attendant physician, etc.

As emphasized above, eternal vigilance during the period of apparent improvement is absolutely essential to the safety of the patient. No physician should see a patient through an attack of appendicitis without the assistance and counsel at all stages of an experienced surgeon.

When peritonitis is general an immediate operation offers the best chance of recovery. When an operation is for any reason not practicable, the patient should be kept deeply under the influence of opium. Hypodermics of morphin offer the surest means of narcotizing the patient. The number of respirations should be brought down to twelve or less a minute. If there is no vomiting, tincture of opium may be given in large doses by the mouth (see Peritonitis). Rectal suppositories of the extract of opium have also been recommended. If there is vomiting the stomach should be washed out with warm water, and this process may have to be repeated every few hours. Hypodermoclysis is invaluable in overcoming shock and adding fluid to the system. Eight to 16 oz. (250 to 500 c.c.) of physiological salt solution should be introduced every six to eight hours. The patient's extremities must be kept warm. Warm applications to the abdomen are often preferable to the ice-bag. Every effort must be made to conserve the vitality of the patient until the surgical intervention is undertaken.

Introducing warm salt solution into the bowel by the Murphy process is often highly advantageous. The physician must bear in mind that, while the treatment of this form of peritonitis is essentially surgical, the fate of the patient is often determined by factors which are not surgical;

that surgical intervention is an incident in the treatment, but does not constitute all of the treatment, and, finally, that exceptional cases clear up without surgical intervention.

Appendicitis in Typhoid Fever

The appendix is so frequently affected in the course of typhoid fever that the question of operative treatment will often have to be considered. So many cases of successful operative interference have been reported that a discussion of the desirability of such interference is in order. An extensive experience with "the typhoid appendix" both in the wards and as pathologist of the City Hospital has convinced me that an operation for the typhoid appendix is rarely called for.

Kelly gives a most enlightened discussion of this subject, and the following quotation from his monograph covers the question most conclusively:

"In a case of suspected appendicitis with an alternative diagnosis of typhoid fever the wisest course is to wait. The best general rule is not to operate for appendicitis in the early stages of typhoid fever—say up to about the tenth day—in the absence of exceedingly urgent symptoms; give the patient the benefit of the doubt, wait, and watch closely. The clinical history of the collected cases seems to show that, with the rarest exceptions, there is no more occasion for operating a true typhoid appendix than there is for cutting down upon the ileum and excising the affected Peyer's patches."

This rule of delay, except in extreme urgency of symptoms, accords with the established practice of some of our best operators. J. B. Murphy of Chicago, for example, in a personal communication, says:

"It is my opinion that typhoid appendicitis should not be operated upon unless there is a perforation. All my cases recover, those operated and not operated. At the same time I feel that operation should not be performed except in special cases."

There prevails in some quarters a strong tendency to operate in typhoid fever as soon as symptoms of appendicitis appear, this course of action being encouraged by the swollen condition of the appendix as found, as well as by the favorable outcome of the operation. The surgeon in such a case congratulates himself that he has obviated a serious complication of the disease at what he considers little or no risk to the patient. This would be the case if the microscopic appearance of the typhoid appendix had the same significance as that of an ordinary inflamed appendix, but experience shows that this is not true. The inference that a swollen typhoid appendix must shortly advance to gangrene or perfora-

tion is not warranted by the well-established facts. *Per contra,* when, after a siege of pain in the right iliac fossa, the patient lapses into an ordinary typhoid, with an entire subsidence of the severe local symptoms, the observer must not hastily conclude that he was wrong in suspecting an involvement of the appendix in the first instance. The autopsy records show, as I have said, that the appendix is often much swollen, but that this condition is a frequent accompaniment of the early stages of the disease.

When, however, the severity of the local symptoms is such that a perforation seems probable, the surgeon should not hesitate to operate without further delay. Under these conditions, says Kelly, minutes rather than hours should be counted as precious.

"If the operator is familiar with the endermic use of cocain in surgical operations, he will often do better to open the abdomen under a cocain or a cocain-adrenalin solution than risk the dangers of struggling and the depressing influence of a general anesthetic.

"It is best to make a free incision in the right semilunar line and evacuate all purulent and fecal material, after which the appendix can be tied off at its base and removed. If necessary other incisions may be made for more efficient direct drainage."

Appendicitis Complicating Pregnancy

Attacks of appendicitis during pregnancy are not uncommon. The earlier they occur in the course of the pregnancy the easier they are to recognize and the less dangerous to treat. Every woman who has appendicitis during the childbearing period of life should have a prophylactic appendectomy performed. Should pregnancy ensue before this has been accomplished, the woman should be guarded most carefully, and upon the first signs of recurrent appendicitis an operation should be made. Appendicitis becomes more dangerous as pregnancy proceeds. During the first four months of pregnancy a prompt operation is safe, and has only a slight tendency to produce an abortion. If at all possible the abdominal opening should be closed, as drainage tends to cause premature labor. Delay in operating greatly increases the risk to mother and child. Suppuration in advanced pregnancy is very dangerous; the maternal mortality is about 50 per cent; the fetus may die, but it is usually born alive. Medical treatment is entirely out of place. Even should the attack subside under medical care, the subsequent changes brought about by pregnancy and labor may cause serious or fatal complications.

A definite attack of appendicitis, therefore, occurring during pregnancy and recognizable as appendicitis, is an absolute indication for immediate surgical intervention. During the first few days of the puerperium appendicitis simulates puerperal sepsis. If a diagnosis can

be made an operation is indicated. In the absence of certainty a conservative course is justifiable.

CHRONIC CONSTIPATION

Chronic constipation may be defined as a pathological condition characterized by insufficient fecal evacuation. The insufficiency may refer to the quantity evacuated or the frequency of evacuation. From a practical standpoint we may divide constipation into two groups: (1) habitual constipation without anatomic abnormality; (2) obstipation, in which the constipation is due to mechanical obstruction or to interference with peristalsis.

It is possible to subdivide these groups into many minor divisions, depending upon the underlying cause of the insufficiency, or the place in which the feces are delayed, or the quantity or quality of the feces themselves, or upon the particular nervous or muscular defects. For the present purpose, however, the simple classification will suffice.

Habitual Constipation

In the vast majority of cases habitual constipation is purely functional in character, that is, absolutely independent of anatomical conditions or pathological changes in the digestive canal. It is nearly always an acquired disorder and due to causes which are very well understood. Certain general causes have led to the gradual increase in constipation, so that its prevalence is almost coextensive with civilization. Spivak has pointed out that "the tendency of civilized life in general and of modern dietetics in particular is toward the production of lesser quantities of fecal matter and less frequent intervals of evacuation." He calls attention to the fact that at no time in history have civilized nations consumed so much meat and eggs, so much prepared and partially digested foods; and the greater efficiency of the dental art has contributed its share to the reduction in the quantity of fecal matter. City life is more conducive to constipation than the more active country life; and the great increase of the more sedentary occupations has led to the same results.

Aside from the general causes, constipation is usually acquired under conditions which are more or less directly under the control of the affected individuals themselves. Women as a class suffer much more frequently from constipation than men. This is the result of many causes. Many women eat too little food or too concentrated food; they drink too little water. They exercise little or not at all. Their style of dress inhibits the activity of the abdominal organs. Pregnancy weakens the power of the abdominal walls, and parturition often results in injury to those

muscles which are actively concerned in the act of defecation. Many women are led by a sense of shame, or as a matter of convenience, to repress the calls of nature, so that the sensitiveness of the rectum to the physiological stimulus of defecation becomes blunted. This cause is especially active during the school years and the adolescent period of life, and is probably more than any other one cause the predominating factor in the production of habitual constipation. Chlorosis and atonic states are also prevalent at this age, and not only blunt the sensitiveness of the nerves, but also reduce the muscular power of the individuals. Men often become constipated as the result of traveling, the inconveniences of a traveling life often leading to a suppression of the calls of nature. Overindulgence in tobacco may have a similar result, and the habit of reading while at the toilet, though often beneficial, sometimes so blunts the sensitiveness of the rectal nerves that they fail to respond properly.

The moderate irregularity in the periods of defecation brought about in the various ways described above would not of itself be of great importance were it not followed by a chain of other events. The individuals under consideration follow one of two courses. They may at first pay no special attention to the irregularity which increases and brings in its train certain secondary symptoms, such as headache, biliousness, loss of appetite, fullness in the abdomen, etc. On the other hand, easily alarmed by the failure of the bowels to act, they resort at once to laxatives, choosing remedies which they see advertised or which are recommended to them by their friends. Finding themselves promptly relieved in this fashion, they again make use of the chosen remedy at the first suggestion of constipation, and thus very easily the "pill habit" is acquired. The bowels now refuse to act without the added stimulus of some drug and the habit assumed so easily becomes fixed upon the individual. In the course of time the strength of the pill has to be increased and the resort to stronger and stronger remedies often results in an uncomfortable state, in which natural unaided defecation becomes impossible.

It is necessary to discuss the etiology thus in detail because a consideration of these features suggests at once the proper prophylactic and curative measures. Like all functional troubles, constipation is far more readily remedied in the beginning than when it has become a fixed habit. It becomes the duty of the physician to find out which of the etiological factors is the most important, and to counteract its influence. In addition every constipated patient should be taught enough of the physiology of digestion to estimate rightly the necessity for regular evacuations and the means of bringing about this result. It is surprising what simple remedies will produce the desired effects in certain cases. Simply increasing the quantity of drinking water or taking a glass of cold water at bedtime and in the morning may suffice. Reducing the quantity of tea consumed or stopping it altogether, increasing the amount of fruit, the addition

of stewed prunes or apples to the dietary, any of these means may bring about daily evacuations in the incipient cases. Other patients may require more active measures, such as outdoor sports, swimming, horseback riding, tennis, baseball, abdominal massage, and various gymnastic or calisthenic exercises. Others can correct the tendency to constipation by going to the toilet each day at the same time and making an honest and persistent effort to evacuate the bowels.[1]

While any of the just mentioned simple measures may suffice in the incipient cases to overcome the constipation and lead to daily evacuations, the more confirmed cases require far more systematic and active treatment to bring about a cure.

These confirmed cases of habitual constipation without anatomical defects are often divided into various groups, among which the spastic form is distinguished from the atonic, and among which can be recognized the types due to the overutilization of the food (Schmidt) and to imperfect digestion.

There is no doubt that a spastic form of constipation exists; that it can usually though not always be clinically recognized; and that it requires certain lines of treatment peculiar to itself. On the other hand, it is held, not without justice, that the spastic form has no absolutely pathognomonic signs or symptoms; that the dietetic treatment proper to the atonic form usually suffices to cure the spastic form, and, therefore, we are not warranted in putting the spastic variety in a class by itself. This will be discussed more fully later on.

Schmidt, who has done so much to further the scientific study of intestinal disorders, has advanced the theory that the term functional or essential constipation should be reserved for a class of cases in which the constipation is due to too little fecal residue on account of the overutilization of the food. In a recent publication he calls attention to the fact that different healthy individuals differ enormously in their ability to digest vegetables.

Many people digest without visible residue all sorts of raw and ordinarily indigestible plant foods, while others pass unchanged even well-cooked vegetable foods. Schmidt has furthermore demonstrated the great influence of the HCl of the gastric juice on the digestion of vegetables. The HCl loosens and partly digests the so-called "middle layer" within the cellulose sheath, but between the individual vegetable cells, so that the vegetable cells can the more readily fall a prey to the alkaline digestive juices of the intestine. The more HCl in the stomach the better the vegetables are prepared for intestinal digestion. Schmidt thus explains the well-known association between hyperchlorhydria and constipation. Thorough cooking also tends to loosen up this middle layer, but never so

[1] Suggestive measures are very useful and efficient in many of these patients.—Editor.

thoroughly as do the chemical juices of the gastric and pancreatic secretions. The combination of good cooking and "too good" a digestion or even too good a digestion of and by itself is the cause of an important type of functional constipation. Moritz, von Noorden, Naunyn, and Einhorn have expressed the opinion that the insufficiency of fecal residue is not the cause of constipation, but the result, the food materials remaining in the bowel so long that they fall a prey to bacterial decomposition.

Schmidt answers this view by calling attention to the fact that the stools of constipated persons contain fewer bacteria than those of healthy persons, and that they likewise contain none of the products of bacterial decomposition. The practical points to be drawn from this discussion are the necessity for using large quantities of plant foods in cases of hyper chlorhydria if they are to be cured of their accompanying constipation by dietetic methods alone; and the advantage of adding substances to the diet (such as agar, regulin) which will materially increase the bulk of the fecal residue.

On the other hand, Hale White calls attention to a class of patients past middle life, who are of sedentary habits and who exercise too little and eat too much. These patients are apt to be constipated and are best treated by reducing the quantity of food while increasing the amount of exercise and fresh air. These patients often suffer from constipation during the winter months, but have regular evacuations during the summer when they indulge in golf or other outdoor sports. A regular annual or semi-annual visit to a mineral spring is often of the greatest benefit to these patients.

Leaving these special types and all theoretic considerations aside for the present, we can group the vast number of cases of functional constipation into two clinical classes:

Class 1 includes those who are curable by an appropriate regulation of their diet.

Class 2 is made up of those who, in addition to dietetic rules, require treatment of a medicinal or mechanical kind to increase their muscular power, their nervous energy, and their general vitality.

The treatment of constipation by diet alone is successful in the large majority of instances. The methods by massage, hydrotherapy, electricity, etc., etc., described at great length in the textbooks and special treatises, are fortunately superfluous in the general run of cases. This fact should be distinctly understood, and every physician can hope to deal with this class of patients successfully without being armed with a great array of instruments and special devices. Only the minority of patients will fall under Class 2, and these can usually be directed to adopt certain lines of home treatment which almost uniformly bring about the desired results.

The treatment by diet is based on the observation that certain foods

and certain combinations of foods have a stimulating effect on intestinal peristalsis. In a general way all foodstuffs can be divided into two classes: those which tend to produce constipation, and those which favor the movement of the bowels. As is well known, the albuminous foods tend rather to constipation, the vegetables and fruits to catharsis. Those foods which leave little residue after digestion have correspondingly little value in the treatment of constipation, and their use should be greatly limited or altogether excluded. Among these are meat, eggs, cheese, spaghetti, macaroni, milk, cocoa, chocolate. Certain foods have objectionable astringent properties, such as India or Ceylon tea, red wines, and blackberries, and they should be eliminated from the diet. The foods which favor catharsis may do so as a result of a laxative principle, or simply because of the bulk of their indigestible residue (chiefly cellulose). Those with a laxative effect are most of the fruits, especially oranges, grapefruit, apples, prunes, watermelon, grapes, peaches; some of the vegetables, such as tomatoes, cucumbers, potatoes, carrots, beets, garlic, onions, spinach. Certain foods, such as honey, buttermilk, cresses, syrup, cider, and certain acid wines are decidedly laxative. The foods with a large residue are the coarser grains, such as rye, oatmeal, and corn, cabbage, Brussels sprouts, turnips, string beans, kale, peas, rutabaga, oyster plant, squash, etc. Mineral oils are laxative; butter, vegetable oils, suet, and cream all favor peristalsis. Water, when freely taken, is an aid in overcoming constipation. Some people are constipated because they take too little fluid, or because they perspire so freely that the feces become hard and dry. In these cases plenty of water is curative. Hard water is constipating and must be avoided.

The judicious mixing of various foods is a valuable means of overcoming constipation. Buttermilk, for example, when taken by itself or as a sole article of diet, may be actually constipating; yet when taken in combination with other foods it may be decidedly laxative. It will not do, however, to allow an entirely unrestricted mixing of various foods. Experience has taught that certain restrictions are necessary, and that gastritis and enteritis can easily be produced by indiscriminate combinations. For example, ice cream and sour fruits, beer and fruits, cucumber and iced water, soda water and fruit acids (especially ice cream soda with acids) are all irritating mixtures and may be followed by vomiting or diarrhea.

For a number of years I have prescribed with gratifying success a diet along the following lines: On arising, 1 glass of cool water. Breakfast: oatmeal, whole wheat or Graham bread, butter, coffee with cream and sugar, raw or cooked fruit or marmalade. Forenoon: 1 glass of buttermilk. Luncheon: fruit, at least 2 vegetables, coarse bread and butter. Afternoon: 1 glass of buttermilk. Dinner: fruit, at least 2 vegetables, coarse bread and butter, salad, suitable dessert. Bedtime: 1 glass of but-

termilk. The noon and evening meals are interchangeable. A small portion of meat or fish or sea food may be taken at either meal. Sardines, herring, mackerel, and shad are especially suitable. Cider may often be substituted advantagenously for the buttermilk. It is surprising to note the immediate effect of such a diet. Many patients who for years have not had an unaided movement of the bowels begin at once to have daily evacuations. The continuation of this diet for weeks will usually have the effect of accustoming the bowels to regular activity so that later the patients may adopt any diet without relapsing into a constipated state. Many persons are entirely willing to adhere to the diet indefinitely. Like all other therapeutic resources the anticonstipation diet must be "mixed with brains" and will require many modifications to suit individual needs and conditions. Some patients will not be able to take such a varied allotment of acid fruits without suffering from dyspepsia and intestinal flatus. It is remarkable, however, that many persons with marked hyperchlorhydria are able to adopt this diet without discomfort. Should the acids cause heart-burn or gastric irritation an alkali can sometimes be taken with advantage one hour after the three principal meals. A mixture of calcined magnesia and sodium bicarbonate is especially suitable, and can be withdrawn gradually as the patient becomes accustomed to the diet. Delicate women cannot always manage to eat the varied assortment required.

In these subjects other methods, such as massage, exercises, and cold rubbings, must be used as adjuvants during the early weeks of treatment. A few diet schemes suggested by other authors are appended. E. I. Spriggs recommends the following: Breakfast: porridge and golden syrup, fat bacon, whole meal bread, butter, marmalade or honey, coffee with cream. Luncheon: fish, potatoes, green vegetables, salad with plenty of oil, stewed apples or figs, water or lemonade, whole meal bread, butter, 1 orange. Tea: weak, freshly made China tea with cream, whole meal bread and butter, jam or honey, gingerbread. Dinner or supper: tomato or other vegetable soup, meat, spinach, French beans, asparagus, salad with oil, dry toast or biscuits, apple charlotte, stewed pears or prunes, water or lemonade, cheese, grapes, or other uncooked fruits.

Zweig gives several excellent diets for spastic and atonic constipation. They do not differ essentially from each other. He advises the following diet to cure habitual constipation, and adds that in no other department of medicine are dietetic rules crowned with more uniform success. Upon arising: a glass of cold water containing a pinch of salt, or fresh fruit (orange, apple, melon). Breakfast: tea or coffee with milk, Graham bread and butter, honey or marmalade. Forenoon: 1 glass of sour milk, buttermilk, or one-day-old kefir, rye bread with butter, and a herring or Graham bread with sardelle butter. Noon: no soup; radishes with butter; a little meat or fish, salad, pickles, and a variety of vegetables, stewed

fruit with a tablespoonful of sugar of milk, dessert with fruit juices, cider with a tablespoonful of sugar of milk. Afternoon: tea or coffee with milk, Graham bread and butter, marmalade. Supper: meat or eggs, pickles, salad or vegetables, raw fruit or preserves, Graham bread and butter, soft cheese, cider. 10 P. M.: stewed prunes or a glass of one-day-old kefir.

Naturally, these diet schemes must be adapted to each individual's tastes and digestive capacity. Almost all lists follow the same general plan. If the lists are suitably modified the result will be successful in the large majority of cases. Failure to cure by dietetic means alone in the purely functional cases is due to a variety of causes. Chief among these is a general atonic state of the individual which prevents him or her from using so coarse or mixed a diet. In these cases the patient must be gradually toned up by constitutional treatment, by local and general massage, and by exercise, and during this period recourse must be had to mild laxative drugs or mineral waters.

For these patients Hale White has advised the following régime: A diet should be used which approximates as nearly as possible the ones advised above. Daily exercise in the open air is necessary. Every morning a simple aperient should be used in a dose just sufficient to move the bowels. Nux vomica is a desirable addition. Before arising the patient must have her abdominal muscles massaged thoroughly for fifteen minutes, more or less; she may also train her abdominal muscles by certain exercises which will be described later. An abdominal supporting bandage is often advantageous. In two or three months the aperient may be gradually reduced until it is no longer necessary, but the massage and exercises should not be omitted until spontaneous movements of the bowels are obtained. If the feces accumulate in the pelvic colon or rectum simple enemata may be necessary, but one must guard against becoming addicted to their use. A glycerin suppository is often preferable to the enema. White says his successes are so uniform with the above method that he can scarcely recall a failure—though in severe cases many months of perseverance are required to effect a permanent cure.

Mechanotherapy.—Many volumes have been written on the treatment of constipation by various mechanical means, such as massage, electricity, gymnastics, hydrotherapy, and surgical procedures. The general practitioner must learn to regard these numerous methods in a proper perspective. *In the general run of cases they are superfluous; in a large number of cases they are helpful, though not essential; in a small proportion of cases they play an indispensable rôle in the treatment; in not a few cases they are meddlesome and, therefore, contra-indicated.*

In debilitated, neurasthenic, housebound, or bedridden patients they have their appropriate field of usefulness. They are largely empirical. "By no stretch of imagination," says Dowse, "can mechanotherapy be

classed as an art or a science." Mechanotherapy acts by directly stimulating the muscles and nerves, by increasing the local circulation, and, indirectly, by suggestion.

Massage.—Massage is the most useful of the mechanical means of overcoming constipation. The movements embrace: (1) effleurage; (2) petrissage; (3) friction; (4) tapotement; (5) vibration. The best time for the massage is in the morning before breakfast. For the technical details the reader must consult the special textbooks on the subject. The manipulations are made from the cecum to the sigmoid flexure. Especial attention must be given to the hepatic and splenic flexures, the left inguinal region, and to parts above the navel (Dowse). "The pressure movements," says Dowse, "to be effective must be gliding, slow, purposive, and well maintained."

Einhorn advises against massage in cases of spastic constipation. In the atonic variety he considers it useful. According to him, it should be given every other morning for at least six weeks. Other authors advise its use daily.

There is no doubt that treatment by massage, if persisted in for many months, is successful in many cases, but, as stated above, the massage should generally be considered merely an auxiliary to the treatment by diet and exercise. Automassage may usually be practiced by the patient with benefit. This may be performed with the hands or by means of the well-known cannon ball covered with leather or flannel, or left uncovered. The cannon ball was first suggested by Sahli; it should weigh between three and five pounds. The patient kneads the muscles in the direction of the colon, devoting most pressure and time to the cecum and the region of the flexures.

Physical Exercises.—Next to diet, physical exercises play the most important rôle in the treatment of functional constipation. In fact, it may be stated that very active persons are rarely constipated. Outdoor sports, whenever practicable, should be given the preference. Most authors extoll the virtue of much walking. It is my experience that walking of and by itself rarely brings about a cure. More active exercise is necessary. In young people baseball, tennis, rowing, swimming, and similar sports should be selected. In middle-aged and older patients no exercise excels golf in its beneficial effects.

Caution must be used against overexercising to the point of exhaustion. This is rarely helpful and is often decidedly harmful. The bad effects on the bowels of excessive sweating have already been noted. When outdoor sports are not available, calisthenic exercise and gymnastic training either in a regularly fitted-up gymnasium or at home are most helpful. The parallel bars, the jumping horse, and the pulleys are particularly appropriate. But many men cannot attend a gymnasium and many women are too weak to employ the ordinary apparatus. For them many forms of

calisthenic exercises have been arranged. Their great utility is unquestioned. Aside from the general effect of all exercise in stimulating the general metabolism, stimulating the appetite and the digestive capacity, these special movements tend to strengthen the abdominal muscles and greatly increase the neuromuscular vitality of the whole digestive canal. Gant has excellently grouped the most useful of these exercises as follows:

1. Stand erect with the legs together, and slowly bend the upper part of the body to the left as far as possible, and then to the right in the same manner.
2. Assume the erect posture and rotate or turn the body upon the hip.
3. Take the same position and, without bending the knees, slowly lean forward and downward until the tips of the fingers touch the floor in front of the toes.
4. Lie flat upon a firm bed, table, or couch, with the legs held rigidly together, and raise the body until it is at or near a right angle to the limbs.
5. Reverse the procedure by raising the stiffened limbs until they are at a right angle to the body.
6. While still in the recumbent posture flex the knees and draw the thighs closely up against the abdomen.
7. Kneel upon the floor and, with pelvis fixed, bend the body in succession forward, backward, from side to side, and then rotate it as far as possible first in one direction and then in the other.
8. Standing erect, with hands crossed behind or extending fully above the head, quickly change to the squatting posture.
9. Lean slantingly forward and repeatedly draw up the abdominal muscles, and then relax, taking deep respirations, to exercise the diaphragm and the abdominal muscles.
10. Extend both arms at a right angle from the body, so as to form a straight horizontal line, and, with the arms held in this position, walk six or eight times on tiptoes from one end of the room to the other.

The above movements should be repeated from five times for the beginner to ten times for persons accustomed to the exercise, and are more effective when practiced systematically, the one after the other, and for a period of time varying from fifteen minutes to one-half hour.

In the beginning once daily is sufficient, but later on they may be carried out twice daily, and, as a rule, if persisted in, they become a habit, and the exercise is looked forward to with pleasure.

Electricity and Vibratory Massage.—Of all the physical means used in the treatment of constipation electricity is the least reliable. In the hands of any but the most expert electrotherapeutists it is almost sure to fail. Even in their hands it must be looked upon merely as an auxiliary measure in connection with treatment by diet and exercise. It is true that per-

sistent treatment by electricity may succeed in bringing about normal evacuations in time, and even that remarkable success is achieved in a short time in exceptional cases, but these results in no way militate against the general conclusion that electricity is not to be considered a routine measure in the treatment of constipation. It is unfortunate that authors continue to reproduce at great length the various methods of treatment by electricity and to describe in detail the instrumentarium which is necessary. Personal experience over a period of many years has convinced me of the comparative inutility of electricity, except by way of suggestion. Gant, who devotes fifteen pages to the electrical treatment of constipation, says that when employed alone it will fail to give permanent relief in a large percentage of cases. Musser and Piersol state that electricity is the least useful of all the physical methods. Mummery says that the small galvanic and faradic batteries employed in the treatment of constipation are quite valueless, but he recommends the three-phase sinusoidal current, the continuous current with quick reversals, and the high-frequency current, if properly applied. The small-roller electrode, which is commonly used with either the faradic or galvanic current, acts in the same manner as simple massage or the cannon ball. The reader is referred to the numerous treatises on electrotherapeutics for a description of the great variety of methods recommended by different authors.

Vibratory massage acts partly by suggestion, partly like simple massage. The instrumentarium is cumbersome and costly, the technic exacting, and the treatment, to be successful, must be combined with other methods. When indiscriminately employed much harm may be done.

Hydrotherapy.—Hydrotherapy is to be considered merely an indirect method of treating constipation. It acts by its stimulating effects upon the nerves and muscles of the abdomen and the general system. Cold plunges, cold rubbings, spinal douches, and other methods of application all have their appropriate indications. Enemata are useful for their immediate purpose of emptying the colon and rectum. They have no curative influence. Many patients resort to enemata daily for many months or years with entire satisfaction. As a rule, however, external conditions intervene to make this method inconvenient or impossible, or the enemata gradually lose their effect. Large colonic flushings should never be used for more than a few weeks, or at most months, at a time, as they tend to cause distention and relaxation of the bowel. Too hot water has the same effect. For ordinary use 1 quart of warm water or warm soapsuds is sufficient. For special enemata to meet particular conditions the reader is referred to the appropriate chapters.

Spastic Constipation—Enterospasm.—Spastic constipation may be acute or chronic. In the acute form patients suffer from more or less severe abdominal pain; there is the desire without the ability to evacuate the bowels. The use of cathartics aggravates the symptoms, giving rise to

severe cramps. If purgatives are pushed reflex vomiting may result, and the case may simulate one of intestinal obstruction. The abdomen is usually flat; there is no sign of colonic distention. These symptoms may persist for several days. The treatment must be directed toward relieving the spasm of the colon. Bed rest is a necessity. All purgative medicines are absolutely contra-indicated. Hot applications in the form of Priessnitz compresses or the hot-water bag are exceedingly useful. The colon should be flushed with large quantities of warm water or salt solution. Belladonna is by far the most useful drug. Five or 10 drops of the tincture may be given in hot water every three hours. The following prescription is appropriate:

℞ Tr. belladonnæ		5.0-10.0	min. lxxv-cl
Spt. chloroformi Spt. menth. pip.	āā	10.0	min. cl.
Tr. valeriani q.s. ad		60.0	℥ii

M. Sig.—One teaspoonful in hot water every three hours.

Atropin in doses of gr. 1/100 or 1/150 (0.0006 to 0.0004 gm.) may be given by mouth or hypodermically two or three times a day. Small doses of morphin or tincture of opium are valuable.

The chronic form is not always to be recognized with certainty. The stools are either thin, flat, compressed, ribbonlike, or broken up into small nodular masses. When the bowels have moved the patient has the sensation that the evacuation has been incomplete. The ordinary purgatives are not effective in producing copious stools. The patient often has irregular pains along the course of the colon. The colon either in its entirety or in various segments can be palpated as a hard, cordlike mass. In very thin patients scybalous masses retained in portions of the colon can be felt. The patients belong to the atonic or neurasthenic type.

The treatment of this chronic type differs from that of the atonic form in various ways. All active mechanical treatment by massage, electricity, vibratory massage is here contra-indicated. Physical rest and hot compresses are useful. Colonic flushings are indicated for a time. The oil enemas described in the treatment of mucous colitis are especially valuable. The diet need not differ essentially from that appropriate for the atonic form. General hygienic treatment, fresh air and sufficient relaxation are necessary for a permanent cure.

Soper recommends local treatment in these cases. The patient assumes the knee-chest position. The sigmoidoscope is introduced as far as possible. A well-lubricated soft rubber catheter is passed through the tube and from 1 to 2 oz. of a saturated solution of magnesium sulphate is injected by means of a piston syringe. The sigmoidoscope and catheter are withdrawn, the patient remaining in the knee-chest position for at least

five minutes. These treatments are continued until the spasm relaxes. The results are said by Soper to be brilliant and permanent.

Use of Drugs and Various Special Additions to the Diet.—Drugs are of invaluable assistance in the treatment of many cases of chronic constipation. Many patients are not suitable subjects for treatment by diet or mechanical means. Persons of advanced years can often be made entirely comfortable by the regular use of aperient drugs. The presence of other diseases (cardiac lesions, emphysema, arteriosclerosis, *et al.*) may often contra-indicate dietetic experiments to relieve constipation. People when traveling often have to resort systematically to drugs to regulate the bowels. Finally, many patients not living in their own homes may find it impossible or inconvenient to adopt a suitable dietetic or hygienic régime. All of these patients may be encouraged to obtain daily evacuations by medicinal means. There is a very widespread prejudice against the daily use of laxatives. This prejudice is well founded, but when erected into a principle is entirely without justification. Self-drugging, as pointed out above, leads almost inevitably to certain abuses, but the systematic use of drugs under intelligent guidance is objectionable in theory only. Persons object to "becoming enslaved to the use of drugs," but it is hard to choose between the liberal use of certain fruits on the one hand and the employment of the active principle of certain fruits on the other. While it is not ordinarily judicious to advise any young person to adopt the steady use of drugs for the relief of constipation, this advice in preference to any other may often be given to adults.

I know of several patients who have used the same aperient pill uninterruptedly for fifteen to twenty years with entire satisfaction. Many patients who adopt a dietetic régime for constipation may have to use aperients during the first few weeks until the exercises, the massage, and the diet become effective. The medicines may then be gradually withdrawn. For these and other reasons an intimate knowledge of the action of the usual laxative remedies is of the utmost importance. The drugs which have especially demonstrated their usefulness over a period of many years are senna, aloes, rhubarb, and cascara sagrada. Other popular remedies are podophyllin, phenolphthalein, and magnesia. Senna is very widely employed, and forms the basis of most of the teas in popular use. It has a decided tendency to gripe. When it does not gripe its continued use often produces a tender condition of and a sense of soreness in the bowels. Many patients get good results by chewing from ten to twenty-five senna leaves before retiring; or the like number of dried leaves can be crumbled up in prune juice or other cooked fruit. The compound licorice powder is a preparation of senna which causes pain in some patients, but which acts favorably in others. It is especially suitable in old people, who often take it night after night for months or years. Compressed tablets containing 20 gr. (1.3 gm.) of the compound licorice powder are

useful. Many of the widely advertised laxatives for children owe their potency to senna.

Aloes and aloin are widely employed. Aloin in doses of gr. ½ to 1/6 (0.03 to 0.01 gm.) is used in countless combinations in the ready-made pills on the market. The ordinary combination with belladonna and strychnin, though extensively used, does not seem a rational one, nor is it especially useful. The extract of aloes should be given in doses of gr. i to iv (0.06 to 0.24 gm.), and may advantageously be mixed with extract of hyoscyamus, gr. ss (0.03 gm.). The objection often raised against aloes and aloin, that they irritate the lower rectum, is not a valid one when they are given in moderate doses. Rhubarb has certain advantages and certain disadvantages. In large doses it often irritates the bowel if used for any length of time. In small doses it soon loses its effects. The powdered root may be given in doses of 4 to 6 gr. (0.24 to 0.4 gm.) after each meal, preferably mixed with sodium bicarbonate. A formula especially useful in constipation associated with gastric atony is:

℞	Rhei	10.0	(℥iiss)
	Sodæ bicarbonatis	30.0	(℥i)
	Eleosacchari anisi	10.0	(℥iiss)

M. ft. pulv. no. xxx.

Sig.—One powder after meals two to three times daily.

The pil. rhei composita may be given nightly in doses of gr. ii to iv (0.12 to 0.24 gm.) or in smaller doses, combined with other laxatives.

An excellent dinner pill is the following:

℞	Podophyllin	0.12	(gr. ii)
	Ext. colocynth co.	1.2	(gr. xviii)
	Pil. rhei co.	0.8	(gr. xii)
	Ext. hyoscyami	0.4	(gr. vi)

M. ft. pil. no. xii.

Sig.—One immediately after dinner every evening.

This, like many other formulæ containing podophyllin, acts better when taken immediately after the evening meal than at bedtime.

Cascara sagrada enjoys a wide popularity with the profession and the laity. It produces stools of normal consistency, usually without pain; it does not easily lose its effects, and it has no contra-indications. The dose may be gradually lessened without loss of effect, and in some cases it has been entirely withdrawn by slow degrees and the patient thus rendered independent of drugs. Success by this method is exceptional rather than the rule. The bitter fluid extract is active in doses of from 10 to 60

drops; the aromatic elixirs and fluid extracts require from two to four times this dose. I have found the solid extract in doses of from 2 to 10 gr. (0.12 to 0.6 gm.) quite unreliable. Podophyllin is an undoubted cholagogue of merit. The best dose is from ⅙ to ¼ gr. (0.01 to 0.015 gm.); larger doses should ordinarily be avoided; smaller doses are often ineffectual. It is best mixed with other remedies, as in the formula given above.

Phenolphthalein, though only recently introduced, has been extensively used. It is more valuable in children than in adults. It is apt to produce soft stools, and, in my experience, is not suitable for prolonged use. It has few or no advantages over other better established drugs. Magnesia is very valuable in cases of gastric hyperacidity. In fact, many cases of constipation are intimately associated with, if not dependent on, hyperchlorhydria, and may be cured by the treatment for that condition. Both olive oil and magnesia are especially useful under these circumstances. The chief objection to magnesia is that it tends to produce soapy stools with intestinal gurgling. Physostigmin is a powerful stimulant of intestinal peristalsis. It should be employed with extreme caution, as it is apt to produce enterospasm and congestion of the bowel. Eserin salicylate may be given hypodermically in doses of gr. 1/60 to 1/30 (0.001 to 0.002 gm.) to stimulate peristalsis, but its effects must be closely watched.

Sulphur is a laxative of value. It is usually combined with cream of tartar. It is easily taken stirred in a little cold milk, which disguises the sulphur taste. It is recommended by Hilton for patients afflicted with hemorrhoids. One or more teaspoonfuls may be taken at bedtime. It often produces griping when continued for any length of time.

The salines are useful for their temporary effects, but they are much abused by constipated patients. When taken in large doses they are usually followed by constipation. The best plan is to take small doses about one-half hour before breakfast, although some patients get better results by taking them at bedtime. Magnesium and sodium sulphate, sodium phosphate, potassium and sodium tartrate, and various combinations are ordinarily employed. Some patients can continue these remedies daily for years without increasing the dosage, but this is certainly exceptional. Usually the small doses lose their effect or cause gaseous distention of the bowel and much discomfort. While invaluable for specific indications, they cannot be considered in any sense curative. The same may be said of the ordinary mineral waters in common use. Rubinat, Carabaña, Hunyadi Janos, Apenta, Congress, Friedrichshall, Carlsbad, Pluto, and many others are in enormous demand by the laity; they relieve temporary conditions, are rarely, if ever, curative, and in the long run usually have to be abandoned because they produce unpleasant or pathological conditions.

Many unusual plans have been devised for stimulating intestinal peristalsis. Beechwood sawdust, pebbles, sand, flaxseed, mustard seed, and similar indigestible substances are taken in teaspoonful doses, and often produce the desired evacuations by stimulating or irritating the intestinal mucosa. Bran is a popular remedy and is taken by itself or mixed with cereals or made into biscuits. Sterilized bran is now readily obtainable in sealed packages. As much as several tablespoonfuls of the bran mixed with water may be taken at bedtime or with the breakfast foods. Biscuits made up largely of bran to which have been added the watery extracts of senna or cascara are advertised under various trade names. They are all useful in mild cases. Oily substances are useful when taken by the mouth or administered by the rectum. Systematic injections of olive oil, linseed oil, or sesame oil, as described under Mucous Colitis, are often successful in overcoming constipation, especially of the spastic variety. A simple way is to inject 2 to 4 oz. (60.0 to 120.0 c.c.) of olive oil every night with a hard rubber syringe into the lower bowel and to retain it over night. This is a simple method which is sometimes effective, though often useless.

Lipowski has devised a method of injecting melted paraffin into the bowel at bedtime, which has the advantage that it does not soil the bed and that it usually produces a morning evacuation. Naturally, the use of rectal suppositories (glycerin, soap, cocoa butter, gluten, etc.) cannot be extended over a long period, as they soon lose their effect. When given by the mouth the mineral oils are more effective than the vegetable oils because they are less digestible. They act by lubricating the bowel, by adding bulk to the indigestible residue, and sometimes their decomposition products stimulate peristalsis. Olive oil must ordinarily be taken in large quantities; to overcome constipation 1 or more tablespoonfuls after each meal is a moderate dose. Often half a tumblerful at bedtime or on the fasting morning stomach is effective, though a large proportion of patients cannot tolerate large doses, especially during the warm months. Sometimes the dose can be gradually reduced without losing its effect, though this is by no means the rule. Hale White thinks that nearly all patients can be trained to take 1 oz. of olive oil every four hours by beginning with small doses and gradually increasing them. He thinks this remedy especially valuable in the constipation associated with gastric or duodenal ulcers.

Corresponding doses of the mineral oils are more apt to produce evacuations. Liquid albolene or similar preparations can be taken in large doses at bedtime with gratifying results in many cases. One-half a tumblerful can often be swallowed without nausea or eructations.

Agar has become a popular remedy during the past few years. In this country its effects have been carefully studied by Louis Gompertz. He describes it and the method of its use as follows:

"Agar-agar is a simple carbohydrate taken from seaweed. It has the property of absorbing water readily and of retaining it. It resists the action of the intestinal bacteria and enzymes. When eaten it passes practically unaltered to the intestines, where it adds to the bulk of the feces. It prevents the formation of scybalous masses. Agar-agar comes in long strips, which are ground into small pieces, resembling the consistency of a coarse granular cereal. It is to be taken morning and evening, the average initial dose being 15 gm. (½ oz.). It is eaten with milk or cream with the addition of salt or sugar.[2] The dose may be increased or diminished, as the occasion requires."

In a few cases diarrhea is produced. Gompertz does not class agar as a cure, but states that it is a helpful and harmless remedy which may be continued indefinitely. In Germany agar has been strongly recommended by Professor Schmidt of Halle. Mixed with an aqueous solution of cascara sagrada, it has been placed on the market under the name "regulin," and it has been extensively advertised to the laity.

Constipation Due to Obstruction

It is obvious that the plans of treatment outlined above will not result in a permanent cure if some mechanical cause obstructs the passage of the feces somewhere between the ileum and the anus. The most common site of obstruction is the lowest portion of the rectum. Internal hemorrhoids, rectal ulcers, or fissures may cause obstruction by spastic contraction of the sphincters, or, in time, by actual hypertrophy of these muscles. Fecal impaction is a not infrequent cause of obstruction higher in the bowel. The rôle of splanchnoptosis, colonic adhesions, hypertrophy of the rectal valves, etc., is still a matter of discussion, and the problem awaits final solution in the future.

There is a tendency at present to exaggerate the importance of the mechanical factors in the production of constipation. The publication of books on constipation by surgeons is a suggestive sign of the times. Misled by the bulk of surgical literature, the general practitioner is very apt to lose a proper sense of proportion. It cannot be stated too strongly or repeated too often that the vast majority of cases of chronic constipation are purely functional in character, and can be cured by the dietetic and other simple methods already described. The case requiring surgical interference is the exceptional case.

It is a question if colonic adhesions can ever produce constipation without causing other symptoms, such as pain, dragging, signs of partial obstruction, etc. Putting the matter another way, we may say that con-

[2] The agar is more palatable if it is first covered with hot water and is allowed to absorb this.—Editor.

stipation per se without the above symptoms is rarely, if ever, due to colonic adhesions. Operations upon the large bowel for obstinate constipation without the signs and symptoms of partial obstruction are, therefore, rarely, if ever, justified. Hale White expresses himself very positively on this point. He thinks that the importance of adhesions has been greatly exaggerated; adhesions are so common that almost every one ought to be constipated; even when dense adhesions exist, as in chronic peritonitis, there is often very little constipation. He says that he has never seen a patient whom he should have wished to send to a surgeon for operation, because by diet, exercise, drugs, and massage "all cases can either be cured or, at any rate, made so much better that no surgical interference is necessary." Many surgeons take advanced ground on the other side of the issue, and advise operative interference in many cases of pure constipation which resist medical treatment. Mummery thinks even that certain cases of atonic constipation may call for an operation.

Three methods have been employed, namely, appendicostomy, ileosigmoidostomy, and resection of the entire colon. W. Arbuthnot Lane says that, "if pain is not a feature, the division of the ileum within 4 or 5 inches of its termination and the establishment of a lateral anastomosis between the distal portion of this bowel and the sigmoid or rectum is sufficient. If there is much pain, it is better to take away the large bowel as well."

Lane reported 28 cases of excision of the colon for constipation, with a mortality of 33 per cent. Mummery doubts that this operation is justifiable, and prefers appendicostomy, which is a safe operation without risk. It is difficult to see what advantages appendicostomy has over ordinary colonic irrigations in cases of constipation without obstruction.

Section of Houston's valves or valvotomy, as originated by Martin, has been recommended in cases in which the evacuation of the fecal mass seems delayed or prevented by hypertrophy of the rectal valves. The occurrence of secondary hemorrhage or peritonitis has induced proctologists to devise clips or clamps for the severing of these valves by pressure necrosis. Pennington, Gant, and others have invented clips which are easily applied. Valvotomy is rarely followed by permanent results, and it is questionable if it is frequently called for. After the operation the patient must be treated by diet, massage, etc., in order to attain a lasting cure.

Intestinal Obstruction.—Intestinal obstruction may be paralytic in character or may depend on a mechanical obstruction to the onward passage of the intestinal contents. The paralytic form may be reflex, toxic, or essential, in the latter case being the result of shock or trauma during an abdominal operation. Toxic ileus is often a terminal symptom in acute infectious diseases, and is indicative of an approaching fatal issue; there is no successful treatment. Reflex ileus is usually temporary in nature

and follows acute injuries to pelvic or abdominal organs. Paralytic ileus is always a grave condition. It comes on suddenly after the performance of laparotomy, and cannot always be distinguished from the beginning of peritonitis. Its nature can be suspected from the absolute cessation of peristalsis, the absence of sepsis, and its sudden onset during an apparently favorable postoperative course. It should be treated by gastric lavage, repeated as frequently as necessary; hot applications to the abdomen, and stimulating purgative enemata. The patient must be stimulated hypodermatically, the sodiobenzoate of caffein in doses of 2½ gr. (0.16 gm.) every three hours being especially suitable. Atropin sulphate, in doses of gr. 1/30 to 1/60 (0.002 to 0.001 gm.), is often helpful. Of late eserin salicylate in like doses has come into much favor.[3] Pituitrin or an isotonic solution of the physiologically active constituents of the posterior lobe of the pituitary body has come into very general use after operations and in cases of impending or beginning ileus. One-half to 1 c.c. may be injected hypodermatically and repeated in four or six hours. If inflammatory adhesions have taken place, pituitary extracts are apt to do more harm than good.

In cases which go from bad to worse a second opening of the abdomen and the performance of enterostomy may save life. After the enterostomy the eserin salicylate may be injected with a fine syringe directly into the wall of the small intestine, and this procedure is sometimes followed by copious purging.

Mechanical obstruction may be caused by blocking of the lumen of the bowel from within (fecal masses, gall-stones, foreign bodies), or may be due to constricting bands, volvulus, intussusception, adhesions, slits, etc. The most favorable form is that due to obstruction from within, and by far the most frequent cause in this class is *fecal impaction.* The most common sites of the impaction are the cecum and the lower end of the rectum, though the flexures of the colon are sometimes the place of obstruction. In the majority of cases fecal impaction can usually be recognized as such. When the lower rectum is involved the patient usually has great local discomfort; he has the desire without the ability to empty the bowel; there is tenesmus and sometimes severe pain. The constitutional symptoms are mild or may be wanting. A finger introduced into the rectum will meet large puttylike masses which completely block the bowel; only rarely are the fecal masses dense and hard. Sometimes the finger can succeed in breaking down the mass into smaller bits. When this is not possible injections should be used to soften the fecal material. Six or 8 oz. (180 to 240 c.c.) of olive oil, 2 oz. (60 c.c.) each of glycerin and oil, or mixtures of olive oil, glycerin, and turpentine may be used. The ordinary purgative enema, composed of water, 1 pint (500.0 c.c.);

[3] Adrenalin, because of its effects upon the splanchnic circulation, may also be tried. I have had good results follow its administration in 2 cases.—Editor.

Epsom salts and glycerin, of each 2 oz. (60.0 c.c.); turpentine, ½ oz. (15.0 c.c.), is very useful. It is advantageous to use hot soapsuds instead of water in the above formula. Another suitable combination is: glycerin, 1 oz. (30.0 c.c.); castor oil, 1 oz. (30.0 c.c.); sodium bicarbonate, 1 dram (4.0 gm.); water, 8 oz. (250.0 c.c.). These injections may be repeated every few hours until the fecal masses are softened and expelled. Sometimes it is necessary to introduce a rectal speculum and break down the hard feces with blunt instruments and scoop them out with a spoon or dull curet.

When the fecal impaction is in the cecum or at the flexures, the nature of the obstruction can nearly always be determined. A soft, boggy mass can be palpated at the site of impaction; when this is the cecum the tumor is sausage-shaped and quite characteristic; it can be indented by pressure, is more or less movable, and is not painful to manipulation. Very hard masses at the flexures are occasionally mistaken for tumors, though the history will usually be of assistance in the diagnosis.

Copious injections of cottonseed or olive oil in the knee-chest position followed by large colonic flushings are indicated. The patient may take inwardly large doses of olive oil, 2 to 4 oz. (60.0 to 120.0 c.c.), or 1 to 2 oz. (30.0 to 60.0 c.c.) of castor oil, twice daily. Little or no food should be taken until good evacuations are obtained. Under this treatment the impacted feces are softened and begin coming away on the first or second day. This is sometimes accompanied by severe pain and rarely by some shock. The treatment may have to be continued for a week or more, until the colon is completely emptied; after-treatment may be necessary for several weeks. The dislodgment of the hardened feces may sometimes be hastened by abdominal massage or manipulations, but caution must be used not to damage the bowel. In very exceptional cases it is impossible to overcome the obstruction by medical means, and surgical intervention becomes necessary.

Acute Obstruction Due to Strangulation.—This requires for its successful treatment a clear conception of the underlying pathology, a high degree of clinical skill in estimating symptoms, and uncompromising, aggressive surgical interference when it is called for. Unfortunately, these cases do not always come under observation with the diagnosis ready-made. A busy practitioner, unless eternally vigilant, is apt to overlook the nature of the condition in its early stages. Severe abdominal pain in any patient should always receive the most careful attention on the part of the attending physician. Intense pain associated with constipation and vomiting usually indicates a serious condition. The inability of the patient to evacuate the bowels, even with the aid of enemata, the partial or complete retention of the water, *the impossibility of passing flatus,* and a certain degree of collapse are the most striking symptoms. Meteorism is not always present; visible peristalsis is almost invariably absent; physi-

cal signs may be entirely wanting, while the disease insidiously advances. The diagnosis should always be made before the vomiting becomes feculent and before the collapse is life-threatening. The physician should never neglect a careful search for hernia in every suspicious case.

The first need of the patient is relief from severe pain. Morphin should be given hypodermically in doses of gr. ¼ to ⅙ (0.015 to 0.01 gm.); these doses rarely suffice to give entire relief, and they must be repeated once or oftener. The danger of inducing dangerous narcosis must not be overlooked; 1/150 gr. atropin (0.0004 gm.) should be given along with each dose of morphin. Care must also be taken not to mask the symptoms by overdoses of narcotics, as a correct estimation of the symptoms is essential in indicating the need of surgical intervention. Some authors advise the administration of tincture of opium by mouth, but the hypodermic use of morphin seems preferable from every point of view. Morphin reduces shock, quiets peristalsis, stops or lessens the nausea and vomiting, and strengthens the circulation. By inhibiting the overviolent peristalsis above the site of obstruction it often prevents a bad condition from becoming worse, and may aid the spontaneous recovery from the strangulation. The comparative well-being induced in the patient by morphin must, under no circumstances, be allowed to deceive the attending physician. He must be guided by more objective conditions, especially the passage of flatus and fecal matter. Morphin should not ordinarily be given after the first eighteen to twenty-four hours. By this time the nature of the case will be quite plain. Either the pain and vomiting will have subsided, the general condition of the patient will be good, gas or fecal matter will have passed from the bowel—under which condition further medical treatment will be permissible; or the patient will still be suffering or anxious, flatus will not have passed, the pulse will be accelerated, the shock still present—under which conditions surgical intervention is called for. In every case of suspected obstruction the physician should have early and continuous surgical counsel, so that the right time for an operation should not be missed.

Among all the rules for the correct treatment of acute obstructions one stands out preëminent. *All cathartics must be absolutely forbidden.* More harm is done by neglect of this rule than in any other way. Cathartics stimulate an overstimulated bowel above the site of obstruction; they increase the pain; they heighten shock; they aggravate the vomiting, and usually increase the degree of strangulation. The patient's chances for recovery decrease as the use of cathartics is pushed. All efforts to move the bowels should be from below. The simple enema should first be used; the so-called purgative enemata described above should then be tried at intervals of three or four hours. If the water is not returned, care must be exercised not to overdistend the colon by repeated injections. Treatment by massage or electricity is mentioned only to be condemned.

Atropin sulphate has been successfully employed in many cases of obstruction. Large doses are employed. If patients are under the influence of morphin, gr. 1/12 to 1/20 (0.005 to 0.003 gm.) may be given hypodermically twice in twenty-four hours; in non-narcotized patients the dose should not be larger than gr. 1/30 (0.002 gm.). Lately eserin salicylate has been used hypodermically in doses of gr. 1/20 to 1/50 (0.003 to 0.0012 gm.). Eserin is a powerful stimulant of intestinal peristalsis, and, in my opinion, is contra-indicated in all cases of mechanical obstruction. Pituitrin is also contra-indicated when mechanical obstruction is present.

Gastric lavage is of great value in all cases in which persistent vomiting occurs, or in which the vomiting assumes an offensive or feculent character. It should be repeated every few hours. Hot applications over the abdomen, especially hot moist cloths (Priessnitz compresses), are often useful in allaying tension and pain.

The question is often asked how long it is justifiable to wait before resorting to surgery. Put in this bald way, the question cannot be answered. Ordinarily it is not safe to wait as long as forty-eight hours. If the initial symptoms do not subside under the judicious use of morphin, it is often advisable to operate within twelve hours after the onset. Were an immediate diagnosis always possible, an immediate operation would usually be in order. It is the uncertainty regarding the gravity of the case during the first day which causes delay. It is better to make this delay too short rather than too long. Many more lives are lost by waiting to be sure than by too aggressive an attack. The ability to estimate the symptoms accurately is often the determining factor. As Zweig says, so long as the general condition of the patient is good, the heart action strong, the pulse slow and of good tension, we may quietly proceed with non-surgical measures. But we must not be deceived by a merely apparent euphoria induced by opium, gastric lavage, or atropin. The nature of the obstruction is also of the greatest importance in considering an operation. Obstruction by a gall-stone or by fecal masses does not require so early an operation as when volvulus or strangulation exists.

Intussusception and Volvulus.—These are more easily recognized than other forms of obstruction. Volvulus affecting the sigmoid often begins after a period of constipation; the pain is usually only moderate; tenesmus is frequent. Vomiting may be absent, though there is usually nausea and often hiccup. The constipation is absolute, neither fecal matter nor gas escaping even after enemata. Localized distention of the bowel in the left lower quadrant of the abdomen is very characteristic. Intussusception occurs usually under the age of ten; in addition to the violent tenesmus there is frequently a palpable tumor in the right iliac region which can be felt either through the abdominal wall or by the finger introduced into the rectum. The modern tendency is to resort to surgical

interference with as little delay as possible in both volvulus and intussusception. Opium or morphin may be administered at the outset in moderate doses; large enemata of warm water may be given; it is even permissible to blow air into the large bowel with a double bulb attached to a rectal tube or catheter in a child; but the physician must bear in mind that valuable time should not be lost, nor should the patient be allowed to become exhausted before recourse is had to operative intervention. An intussusception which does not yield to medical treatment in a few hours is more safely treated surgically than by bloodless methods.

Volvulus is preëminently a surgical condition from the start. Medical treatment is justified only by doubt as to the diagnosis. A presumptive diagnosis is ground enough for operative interference.

Chronic Intestinal Obstruction.—Chronic intestinal obstruction is due to many causes. Adhesions and kinking of the colon or of the lower ileum are common, and are a frequent cause of obstructive symptoms of a chronic and variable nature. The various lines of treatment described in the chapter on Constipation are often effective in reducing the symptoms to a minimum, and in course of time they may disappear altogether. Obstinate symptoms due to firm adhesions and permanent angulations can only be relieved by surgical measures.

The most frequent cause of chronic obstruction in the colon is cancer. In inoperable cases much can be done to alleviate the symptoms. The food should be selected with a view to leaving but little residue.

The bowel should be emptied daily by simple enema. When these fail any laxative which will produce a soft, easy motion is indicated. Regular doses of castor oil are well adapted for this purpose; 1 or more teaspoonfuls may be taken every morning. Olive oil may be substituted, but is not so efficient. Preparations of senna and aloes are very useful. All drastic purgatives and all large doses must be avoided. As the tumor grows patients will be better off if their diet is materially reduced. They live comfortably on strained gruel soups, with a little bread, and gelatins. This reduction in the quantity of food will obviate for a long time the need of narcotics. When these become necessary, codein is to be preferred to opium; morphin in solution is better than opium because less constipating, and morphin by mouth is far preferable to its hypodermic use, which is to be avoided in every case, if possible. The addiction to the hypodermic use of morphin brings with it a train of suffering which is added to that of the malignant growth. Patients who take morphin by the mouth live longer and suffer less than those who use it hypodermically.[4] The value of palliative operations must in all cases be left to the judgment of the consulting surgeon.

[4] Some patients are more comfortable on the deodorized tincture of opium which is much less constipating than morphin and is, perhaps, less liable to be followed by nausea and loss of appetite.—Editor.

VISCEROPTOSIS

It is customary to divide cases of visceroptosis into two groups, the congenital and the acquired. The term "congenital" is in one sense a misnomer. The ptosis, itself, is not inherited but merely the tendency thereto. Neither the stomach, the intestines nor the kidney prolapses before the age of puberty. According to R. H. Smith, at the age of puberty there is a widening of the pelvis and a compensatory narrowing of the waist. In weak, relaxed and badly nourished children, these changes are pronounced and the ptoses are apt to occur along with other changes. There are many reasons why the term congenital visceroptosis should be given up altogether and why the so-called cases of congenital visceroptosis should not be classified as cases of visceroptosis at all. For over twenty years it has been well known that congenital prolapse of the abdominal organs is only a part, and not always an important part, of a condition of general constitutional asthenia. In 1899 Stiller designated this condition as "asthenia universalis congenita," and the same year H. Strauss described it as a "coördinated expression of the constitutional inferiority, *Minderwertigkeit,* of various organs." The term "habitus asthenicus," or constitutional asthenia, has since then become prevalent.

The essential truthfulness of Stiller's presentation as applied to a certain large group of cases is generally accepted. Stiller laid especial stress on the long narrow flat thorax, the small bones, the slight panniculus adiposus, the mobile tenth rib and what he called a vulnerable nervous system. His general conclusion has met with practically universal acceptance, namely, that the symptoms in this type of visceroptosis are not due so much to the visceral displacement as to the vitiated muscular and nervous system of the individual.

Intensive study of the habitus asthenicus has disclosed other constituent elements. Among the congenital defects of development (Williams) are failure of the colon to rotate completely into the right flank; failure of complete fusion between the right mesocolon and the posterior parietal peritoneum, resulting in cecum mobile (Wilms); failure of the layers of the great omentum to fuse. Goldthwaite lays emphasis on the smallness of the spine, and the deformity of the lumbar vertebræ. He also accepts as quite characteristic for this type an abnormal shortness of the large and small intestines. He calls attention to the undersized heart, the small lungs, the slender feet with their unnaturally high arches. Other writers have noted that in this type the female genitalia are often poorly developed.

To the study of structure has been added the study of function. It has been found that in children of this build orthostatic albuminuria is not uncommon; weak digestion and constipation are prevalent; and Uhlman has recently demonstrated that the liver in these subjects is physiologically

inferior, as determined by the ready appearance of galactosuria after giving 30.0 gm. galactose.

As many of these patients show a lessened reaction to pilocarpin, that is, a certain grade of sympatheticotonia, it is possible that lessened hepatic function indicates a vitiated nervous system.

When we sum up these observations we find that we have gathered into one group certain individuals of a particular body-form or habitus who are apt to present some or many of the following characteristics: vulnerable nervous systems of neurasthenic type; weak muscular systems; certain skeletal defects; physiologically weak hearts, kidneys, livers and digestive organs; displacement of one or more abdominal viscera. Chiefly through custom we still refer to these patients as being "cases of visceroptosis," although the malposition of abdominal viscera is only one item out of many. It is in fact not always present, frequently does not play an important part in the symptomatology and may easily become a misleading factor in the treatment if an undue amount of attention is paid to it. The error is commonly made of ascribing offhand any existing digestive disorders to the ptosis as such—especially to assuming that the constipation is the obvious result of the prolapse (although we know that prolapse of and by itself does not produce constipation), and to direct all our therapeutic efforts to changing the position of the viscera by bandages, rest cures and finally by operative procedures.

R. H. Smith has reached interesting conclusions. He examined 109 female children in age from birth to thirteen years. He found that the enteroptotic habit of the adult was definitely predetermined by certain physical characteristics in the growing child—namely, slenderness of physique, lack of fat and muscle, and delicacy of form and feature. Actual prolapse of the viscera very rarely occurs in childhood, but the muscular insufficiencies of later life in enteroptotic women are common in frail children. Smith believes that the habitus is of far greater importance to the enteroptotic women than the prolapse of the viscera which accompanies it, also that the symptoms associated with visceroptosis are due in most cases not to the prolapse, but to a genuine fatigue neurosis. In the majority of cases the patient suffers not because her organs are out of place, but because she has been under some strain and is fatigued or is neurotic from other causes. Smith recognizes in addition to the congenitally predetermined enteroptosis an acquired type which occurs in women who were originally of vigorous frame, but who have acquired prolapsus of the abdominal viscera as the result of childbearing, hard work, or other influences involving muscular and nervous strain. Prolapse in these women is never excessive, and is readily distinguishable from the severer constitutional form.

Many clinicians, especially those with surgical tendencies, take decided exception to this conception of visceroptosis. Rovsing rejects Stiller's

hypothesis and ascribes the occurrence of visceroptosis to two factors only: (1) the misuse of corsets and skirt bands; (2) the changes which pregnancy and childbirth occasion in the intra-abdominal pressure. Rovsing takes the radical position that "all the morbid symptoms and conditions which we find typical in patients with enteroptosis allow themselves naturally and spontaneously to be explained as a result of the ptosis." Rovsing classifies gastrocoloptosis in two divisions: (1) virginal; (2) maternal. The virginal type begins at puberty and results from the abuse of the corset, etc. Gastric symptoms predominate, but are followed by a long chain of nervous and nutritional disorders, which, in extreme instances, may lead to death by inanition. The maternal cases result from childbearing, have few or no gastric symptoms, cause little suffering from nervous disturbances, but have most of their symptoms determined by the prolapse of the colon, which causes constipation, auto-intoxication, and, finally, emaciation and a breakdown of the general health.

Three common observations make it obvious that the symptoms associated with visceroptosis cannot be due solely to the abnormal position of the viscera: (1) many persons whose viscera are prolapsed have no symptoms of any kind; (2) these persons may acquire gastro-intestinal symptoms when subjected to physical or nervous strain; (3) the symptoms may be made to disappear in many instances without paying any attention to the position of the viscera.

All we can say with anything like assurance is that many nervous and debilitated patients have gastro-intestinal symptoms which seem in some way to be associated with and aggravated by a prolapse of one or more of the abdominal organs. We are unable to say in any given case just which symptoms are dependent on general causes and which are due to the abnormal position of the affected viscera. Because a prolapsed stomach is atonic or muscularly weak, we are by no means justified in saying that the prolapse is the cause of the atony. Because a prolapse of the transverse colon is associated with constipation we may not *eo ipso* conclude that the prolapse causes the functional disturbance. In the first place, many cases of gastroptosis exist without gastric atony; in the second, many cases of atony exist without ptosis. Their coexistence in any given case is no argument at all for any causal relationship. In the same way coloptosis occurs in the unconstipated; constipation occurs in cases of normally placed colon. Just what kind of coloptosis or kind of constipation justifies the inference that they are causally related has not been made clear. To assume offhand that certain anatomical abnormalities have produced certain functional disturbances is a sure way of being led astray in a large number of cases.

When we come to study the symptomatology that arises in the course of gastrocoloptosis we are struck by the paucity of demonstrated facts and the lack of agreement among various authors concerning the symptoms

actually due to the prolapse. From clinical observation we may assume that gastrocoloptosis is frequently accompanied by disturbances of the motor function of the stomach and colon, variations in the secretion of HCl, and various painful sensations within the abdomen.

Associated with these symptoms, and often overshadowing them, are a variety of complaints usually described as nervous dyspepsia. Constipation is frequent, and the stools appear as small, hard lumps. Especially in the female do secondary nervous manifestations occur. Under these conditions women have a tendency to undereat; they diet themselves and slowly lose flesh. Gastric fermentation is apt to be present; bloating and belching may become troublesome; neuralgic pains ensue, and the disease may advance to profound neurasthenia.

It is thus apparent that a gastro-enteroptosis rarely, if ever, comes to treatment as an uncomplicated entity. Patients present themselves with the protean symptoms of nervous dyspepsia, and on examination the physician finds the associated visceral prolapse. In some cases it is far better to conceal from the patient the fact that the abdominal organs are displaced, and to attack the symptoms entirely from the side of the nervous system (exercise, suggestion, overfeeding, tonics). In many cases, however, the symptoms cannot be overcome until some support is offered the displaced viscera. It should be borne in mind that every case is a law to itself, that infinite tact and much experience are required to treat this class of cases successfully, and, as Montenuis has well said, many patients must be cured by the physician instead of by the physic—"par le médecin plutôt que par la médecine."

In 1899 I thus summarized the preventive measures:

Children of neurotic disposition and those whose constitutional type predisposes to visceral ptosis should be encouraged to indulge in all outdoor amusements. A rational system of physical exercises for growing girls is one of the needs of the day. Physical training for girls combined with dress reform in its true sense is the road along which progress is to be made. Compression of the thorax during the adolescent years must be reduced to a minimum. A great step in prophylaxis can be taken by the more careful management of convalescence from wasting diseases, especially typhoid fever. Emaciation tends to cause prolapse of the kidneys, the stomach and the bowels. A patient should not be considered recovered from an exhausting disease until he has nearly returned to his original weight. After confinement the abdominal walls should be guarded, not for days, but for weeks and months.

In 1894 Glénard said that successful treatment for enteroptosis was "an abdominal bandage, laxatives, alkalis, and a meat diet."

Montenuis says the indications are to reëstablish (1) the abdominal equilibrium; (2) the gastric functions; (3) the intestinal functions. These indications are fulfilled respectively by the abdominal bandage,

a correct diet, and laxatives. It is impossible here even to summarize the treatment necessary to meet all the indications. The reader is referred to the various chapters dealing with nervous dyspepsia, secretory abnormalities, atony of the stomach and bowels, chronic constipation, and neurasthenia. General hygienic treatment combined with an appropriate diet will relieve a large proportion of these patients. In others, however, the symptoms cannot be treated successfully until their origin in displacement of one or more of the abdominal viscera is recognized.

Regarding the diet, no other rule can be laid down than that it should conform to the muscular and secretory power of the stomach. The hope of adding enough fat to the intra-abdominal tissues to support the viscera is entirely illusory. The two objects of dieting are to restore the gastric and intestinal functions and to bring the patient up to a normal state of nutrition. No schematic dieting is possible. Success will depend entirely on the skill of the physician in adapting the diet to the needs and capacity of the patient. In my experience little is to be gained by abdominal massage, electrotherapeutics, vibratory massage, and other mechanical methods (see the article on Chronic Constipation). Active exercises for strengthening the abdominal muscles are of some use. Not too much must be expected of them.

By far the best single agent for overcoming the symptoms due to ptosis is an abdominal bandage so fitted that it offers support to the anterior abdominal wall and a lifting pressure exerted on the abdominal contents from below upward and backward. Three kinds of abdominal supporters have been successfully used: (1) straight-front corsets; (2) variously designed abdominal bandages; (3) strips of adhesive plaster. Of these the corsets are the easiest to employ, but the least beneficial; the bandages difficult to apply, but, when well fitted, the most satisfactory for permanent use; the adhesive strips of greatest immediate benefit, but unsuited for continuous employment.

The best way of applying the adhesive plaster is that of Rose. He uses zinc oxid moleskin adhesive plaster 1 yard long and 8 inches wide. From the middle of the lower edge two lines are drawn extending obliquely upward to two points on the ends, 2 or 3 inches from the upper edge. The bandage is cut along these lines, and is then in three pieces. The point on the lower edge is now applied just above the symphysis pubis, the plaster carried around the body, and the ends overlapped in the back. The two side pieces are used to reënforce the lower edge of the larger piece on each side.

A much simpler adhesive bandage is described by McCaskey. Numerous other modifications of the Rose bandage are in general use. The chief objections to all bandages made of adhesive plaster are the irritation of the skin and the necessity of renewing the dressings frequently.

I shall not enumerate the various types of bandages designed to support

the viscera. The simple Teufel bandage has many points of advantage. Making windows in the bandage where it passes over the iliac crests is a decided improvement (bandage of Einhorn). Aaron describes a supporter which has many points of excellence. The Storm binder is very practical. Any bandage is useful which applies uniform pressure upward and backward over the hypogastrium and which stays in place.

Surgical Treatment.[5]—Various surgical procedures have been devised to relieve the symptoms of gastro-enteroptosis. In cases of relaxed abdominal wall Gallett, following the example of Depage, Rouffart, Thirar, and Sacré, resected a lozenge-shaped piece from the anterior abdominal wall. Duret raised the prolapsed stomach by suturing its anterior surface to the abdominal wall by a single suture. Rovsing used three rows of sutures passing through the anterior wall of the stomach; he has performed this operation one hundred and sixty-three times to date. Coffee stitched the greater omentum to the anterior abdominal wall, thus raising the stomach and the transverse colon. Beyea elevated the stomach by plicating the gastrohepatic ligament.

All of these operations, in their original or in modified forms, have been performed by a large number of surgeons, but the results cannot be said to be satisfactory. Einhorn tersely says that "ptosis as such does not require surgical intervention." Aaron says that gastro-enterologists have practically ceased to advise surgical treatment for gastro-enteroptosis. Many surgeons are only too willing to try their hand when internal treatment has failed, on the general theory that what cannot be relieved medically must somehow be curable surgically, but Gibson has wisely said that any surgeon operating upon these cases of visceroptosis simply because the physician and patient are tired of each other is sure to do useless and harmful surgery. Discussing the operation for coloptosis, Gibson further says that we are at present apt to wander as far astray in the selection of cases for operation as we formerly did in the case of the kidney. Two difficulties lie in the way of every operation for visceral prolapse. In the first place, nearly all the patients for whom an operation would be considered are neurasthenics, and any operative interference in this class of subjects is apt to be harmful. In the second place it is impossible to state which, if any, of the symptoms are actually due to the ptosis. Thus, it is more than probable that coloptosis per se produces absolutely no symptoms, and that these, if present, are purely neurotic or are due to complications, such as adhesions, permanent kinks, bands, etc. To operate upon cases of gastroptosis and coloptosis, as is done by certain enthusiastic and uncritical surgeons, simply because the patient complains of abdominal symptoms which medical treatment has failed to relieve, is to bring abdominal surgery into sure disrepute.

[5] As a rule patients of this type stand surgical intervention badly. I have frequently seen surgery result in serious aggravation of their nervous symptoms.—Editor.

INTESTINAL NEUROSES

As our knowledge increases, the number of conditions classed as pure neuroses diminishes. There is no doubt that purely nervous disturbances of the intestinal function occur (acute diarrhea, meteorism, peristaltic unrest); it is no less true that many disturbances formerly classed as nervous are due to catarrhal and other pathological conditions of the intestinal mucosa. Cohnheim urges that the diagnosis of neurosis should not be made unless (1) all evidences of organic disease can be excluded; (2) the symptoms are unaffected by dietetic treatment; (3) the symptoms vary with the nervous condition of the patient.

What we call intestinal neurasthenia is usually some pathological condition of the intestine in a neurasthenic individual, and the neurasthenia is often the result and not the cause of the intestinal symptoms. Chronic nervous diarrhea is usually a chronic enteritis or colitis in a nervous individual, and even simple peristaltic unrest and meteorism frequently have their origin in a catarrhal process in the bowel. A rigid and systematic study of the intestinal function should be made in every case before a diagnosis of neurosis is in order.

Very little is to be gained for the purpose of therapeutics by classifying the neuroses into groups, such as motor, sensory, and secretory. The indications for treatment are found not in the more prominent symptoms, but in the etiological factors. Just those symptoms which require specific treatment are due to pathological processes within the bowel, and are not nervous in origin. For example, nervous diarrhea has rather a large literature of its own. The acute nervous diarrhea resulting from fright or worry requires only the removal of the cause to effect a cure. Chronic nervous diarrhea also must be treated from the etiological side, and *dietetic and other restrictions are needed only so far as the disease departs from a pure neurosis and depends on a definite pathological state.* It is decidedly illogical to follow the example of many textbooks of designating a given symptom complex as a pure neurosis, and then laying down a plan of treatment by strict diet, opium, and astringents. The "nervous diarrhea" which requires opium, bismuth, and a proteid diet is not a neurosis, but is due to some disease of the stomach, pancreas, or intestine.

Einhorn describes a case of chronic nervous diarrhea in a neurasthenic patient which was overcome by simply repressing the desire to go to stool. Nervous diarrhea due to pathologic states in the pelvic organs has also been described by various authors. A cure depends on the removal of the diseased organ. Some nervous patients have a desire to empty the bowels shortly after each meal. This is supposed to be due to an excessive neurotic stimulation of intestinal peristalsis. Brunton says it is particularly common in young subjects and highly recommends the use of 1 or 2 drops

of Fowler's solution before meals, or from ½ to 1 teaspoonful of the liquor bismuthi et ammonii citratis. The so-called "morning diarrhea" is not a neurosis, but is due to a catarrhal colitis or to achylia gastrica. Brunton's suggestion that the patient take no fluid after 5 P. M. is a valuable one, but in most cases it is necessary to treat the colitis by an appropriate diet and local irrigations.

Peristaltic unrest and meteorism may be purely nervous in origin, though they are usually the expression of a mild catarrhal enteritis or enterocolitis. Meteorism is sometimes the direct result of surgical shock and may follow abdominal operations or childbirth.

I have seen one neurotic young woman who after each of two consecutive easy and normal confinements had a most pronounced and alarming meteorism without the slightest disturbance of the pulse, temperature, or lochial discharge. The meteorism yielded to hot applications, warm water injections, and the internal use of belladonna. The same symptoms sometimes follow laparotomy and are to be treated as just described.

Peristaltic unrest may result from any disturbing emotional state; it frequently is an annoying symptom during the period of early adolescence. It is to be treated by general hygienic measures, fresh air, exercise, iron, arsenic, and other tonic remedies. It may depend on the ingestion of too many sweets, acid fruits, and badly prepared cereals or leguminous foods. All of these must be prohibited. Charged waters must be forbidden, as well as champagne, cider, soda water. Relief can be obtained by any of the well-known carminatives, by menthol pills, valerian, asafetida, zinc valerianate, Fowler's solution, bismuth. The intestinal antiseptics are not particularly helpful. Charcoal is absolutely useless. Boas recommends the salicylate of magnesia in doses of from 10 to 30 gr. (0.6 to 2.0 gm.) after meals. Belladonna in various combinations is exceedingly useful.

REFERENCES

Aaron. Diseases of the Stomach, 1911.
Bettmann, Henry Wald. The Shape and Position of the Stomach, Phila. Monthly Med. Journ., March, 1899.
Beyea. Phila. Med. Journ., 1903.
Coffee. Ibid., 1902.
Dennet. Med. Rec., Dec., 1911.
Duret. Rev. de chir., 1896.
Einhorn. Med. Rec., July 13, 1912.
Friedlander. Lancet-Clinic, Aug., 1906.
Gallett. La Clinique, Bruxelles, 225-237, 1894.
Gant. Constipation and Intestinal Obstruction, 224, 1910.

Glénard. Introduction to A. Monteuuis, Les Déséquilibrés du ventre, Paris, 1894.
Goldthwaite. Boston Med. & Surg. Journ., June 17, 1915.
Kelly. Appendicitis, 255.
Ladd. Musser and Kelly, Pract. Treat., iii, 491.
Lipowski. Berl. klin. Wchnschr., 1910.
McCaskey. Journ. Am. Med. Ass., Oct. 28, 1911.
Mummery. Diseases of the Colon, 1910.
Rovsing. Arch. f. Chir., 1899.
——— Gastrocoloptosis; Its Pathological Significance and Its Surgical Treatment, Journ. Am. Med. Ass., Aug. 3, 1912.
Schmidt. The Test Diet in Intestinal Diseases, Trans. C. D. Aaron, 1906.
——— Deutsche med. Wchnschr., No. 10, 1911.
Smith, R. H. A Study of Children with Reference to Enteroptosis, Journ. Am. Med. Ass., Feb. 10, 1912.
——— Discussion in Journ. Am. Med. Ass., Aug. 3, 1912.
Soper. Southern Med. Journ., Feb., 1921.
Spivak. Med. Rec., Sept., 1906.
Spriggs. Practitioner, 634, 1910.
Uhlman. Arch. f. Verdauungskr., Nov., 1915.
White. Practitioner, lxxxiv, 599.
Williams. Boston Med. & Surg. Journ., June 17, 1915.
Yates. Surg., Gynec. & Obst., Nov., 1911.
Zweig. Magen und Darmkrankheiten, 1906.

CHAPTER XXXII

DISEASES OF THE LIVER

HENRY WALD BETTMANN

DISEASES OF THE BILE PASSAGES AND GALL-BLADDER

Introduction.—During the past five years our knowledge of the physiology of the liver and of the secretion, storage and flow of the bile has undergone some modification. Some of our older notions concerning the gall-bladder have been given up; some new facts have been added. To understand clearly the principles underlying the treatment of the biliary system it is necessary to have clear ideas concerning the physiology and the pathological physiology of the involved structures.

G. H. Whipple gives an excellent summary of our recently acquired knowledge in *Physiological Reviews* for July, 1922.

The older idea that the gall-bladder is merely a storehouse for bile and that it pours out its contents only during the process of digestion must be abandoned. The flow of bile in most animals, with or without a gall-bladder, is fairly continuous. Factors which influence the flow are stimulation of the duodenal mucosa, foods, nerve stimuli, sphincteric control of the papilla, vascular changes and others. In the human beings the daily quantity of bile secreted is from 500 to 1,000 c.c. In fistula dogs there is little if any decrease in the flow at night. The secretion pressure is low in all animals—varying from 210 to 300 mm. of bile. In cases of obstruction, or of pressure above 300 mm. of bile, absorption of bile takes place chiefly through the liver blood capillaries and relatively little through the lymphatics.

An important function of the gall-bladder is undoubtedly the concentration of bile. Rous and McMaster have shown that the simple passage of bile through the gall-bladder may cause a concentration of the bile to one-fourth or one-half of its original volume. In a twenty-four hour period a dog's gall-bladder can concentrate whole bile to one-fifth or one-tenth of its original volume.

The composition of bile undergoes marked variation under varying conditions. Day by day there is a change in the output of bile salts. This

is largely influenced by diet and little or not at all by cholagogue drugs. The only true cholagogue so far known is the bile salts themselves. Taurocholic acid is more active than glycocholic acid. During fasting periods the amount of available taurin is limited, the supply of taurocholic acid is diminished and the flow of bile is apt to be lessened.

Meat causes an increase in the excretion of the bile acids, though the pigment excretion is diminished. On a meat diet the flow of bile is abundant. Sugar and carbohydrates in general lessen the flow of bile. The greatest concentration of bile is obtained when bile salts are administered with sugar—the excretion of salts is increased, the flow is diminished. Under these conditions the concentration of bile salts in the bile may rise to 7 or 9 per cent by weight.

The duration of the cholagogue effects of bile salts depends on the dosage. After a dose of 1.0 gm. to 2.0 gm. of taurocholic acid the cholagogue effect will cease in from four to eight hours. A dose of from 8 to 12 gm. may prolong the effect from twenty-four to forty-eight hours.

It is doubtful if the so-called cholagogue drugs have real cholagogue effects. Salicylates, pilocarpin, adrenalin, atropin, dilute acids, soaps, glycerin and albumoses have all been classed as cholagogues but their effect is doubtful.

Under certain conditions, and especially after operations, the flow of bile may be inhibited for many hours but the factors underlying this condition are not clearly known.

Irritation of the duodenal mucosa may cause a relaxation of the sphincter of the papilla and be followed by a flow of bile. Meltzer and Auer called particular attention to the action of magnesium sulphate in this connection. According to the so-called law of contrary innervation, relaxation of the papilla was supposed to be accompanied by a muscular contraction of the gall-bladder, causing a pouring out of gall-bladder contents into the duodenum. Upon this rather theoretical assumption Lyon based his much discussed method for the study and treatment of gall-bladder conditions.

Biliousness

Biliousness is a term which indicates a well-recognized and well-defined group of symptoms without postulating any definite pathological process. It follows indiscretions in diet, such as injudicious indulgence in beer, spirits, sweet or greasy foods; it may follow any excessive meal, or, in susceptible individuals, may result from so simple a procedure as taking a nap after a full meal. The attack usually begins in the morning after a restless night, and is characterized by complete anorexia, general malaise, giddiness, headache, muscæ volitantes, and often by nausea, followed by vomiting. The tongue is heavily furred, the urine is highly colored and scanty, the feces are usually scanty and may be ashy gray

in color. In bad cases there may be a subicteric tinge to the conjunctivæ and the general prostration may be intense. Whatever the exact pathological condition present, certain features are prominent. As Wynter tersely puts it, "the digestive apparatus is on a strike." Food, instead of being digested, lies in the stomach until it sets up vomiting. Bile is apt to pass into the stomach and to be ejected by vomiting. The indications for treatment are very simple. The stomach and duodenum must be given rest; the intestinal contents must be evacuated; and, as experience has shown, the excretion of bile must be encouraged. The patient must abstain from all food and drink for from twelve to twenty-four hours. Even sips of water and cracked ice may do more harm than good. Calomel is the remedy *par excellence*. In mild cases it may be given in small broken doses, such as gr. ¼, gr. 1/6, or gr. 1/12 (0.015 to 0.005 gm.), every one-half hour or hour, until 1 or 2 gr. (0.06 to 0.12 gm.) are taken; this is followed in from four to six hours by a saline purgative, preferably Epsom salts. Other salines, such as citrate of magnesia, Hunyadi, or Rubinat water are less reliable and slower of action, but are often employed. Free purgation is usually followed almost immediately by marked amelioration of the symptoms. After the bowels act freely the patient is usually greatly benefited by small doses of the usual coal-tar analgesics, acetphenetidin, gr. v or viiss (0.3 to 0.5 gm.), acetsalicylic acid, salophen, pyramidon, or others. He may also partake of food, beginning with tea and unbuttered toast, this to be followed by simple gruels and clear broths.

Experience has made certain generalizations possible. So long as the patient is actively nauseated it is useless to prescribe analgesic remedies, such as the bromids or the coal-tar preparations. The attack will not pass off until active peristalsis is set up, and the bile stream directed downward instead of upward. Mere emptying of the stomach, either through vomiting or by means of the stomach tube, does not relieve the symptoms, which depend for their continuance on conditions which are infragastric, that is, in the liver itself or in the upper intestinal tract.

In many instances, especially where bilious vomiting is a prominent sign, it is advisable to begin the treatment with salines. The remedy *par excellence* is Epsom salts. This is best administered mixed with fresh lemon juice. A large tablespoonful or more of Epsom salts is mixed in a tumbler with a tablespoonful of lemon juice and not more than 1½ to 2 oz. (50 to 60 c.c.) of cold water are added. The patient to whom Epsom salts is particularly obnoxious may overcome the taste by sucking the lemon before swallowing the draft, which is to be immediately followed by a large tumblerful of cold water. This mixture, which rarely causes vomiting, is usually followed by watery evacuations in one or two hours, and often is a short cut to recovery.

If the physician is summoned in the evening he may with advantage

prescribe any of the well-known "liver" combinations, to be followed by a saline the next morning. A good formula is the following:

℞	Podophyllin	gr. 1/6	(0.01 gm.)
	Extr. hyoscyami	gr. ss to i	(0.03 to 0.06 gm.)
	Extr. colocynth co.	gr. iss	(0.1 gm.)

Sig.—Take at bedtime or immediately after the evening meal.

From ½ to ⅔ gr. of calomel (0.03 to 0.04 gm.) may be advantageously added to each pill. Another excellent formula is the following:

℞	Pil. hydrargr.	gr. iii	(0.2 gm.)
	Extr. aloes	gr. i	(0.06 gm.)
	Extr. hyoscyami	gr. i	(0.06 gm.)

Sig. Take at bedtime; follow with a saline in the morning.

Blue mass given in 5 or 10-gr. doses (0.3 to 0.6 gm.) is useful, but not so reliable as the formulæ just given.

Persons who are subject to bilious attacks may usually prevent them by careful living. Avoidance of all dietetic excesses, of all alcoholic beverages, of all greasy or very acid foods must be insisted upon. Physical exercise in the open air is an excellent preventive. Golf, tennis, and horseback-riding are especially useful. Biliousness often results from fretting and worrying. Late hours, highly spiced foods, mental excitement must all be avoided. The use of one of the above-mentioned "liver pills" immediately after an indiscreet dinner will often prevent biliousness on the following day. Persons who are predisposed to bilious attacks may with advantage take one of the above-mentioned liver pills regularly once or twice a week as a preventive.

Jaundice

Acute Catarrhal Jaundice.—Catarrhal jaundice frequently begins with the symptoms of acute gastritis. There is no reason to disbelieve the general view that the jaundice is caused by a duodenal catarrh accompanied by a swelling of the mucous membrane of the papilla of Vater. Pain is occasionally a prominent initial symptom, and must be relieved by hypodermics of morphin. The treatment during the first few days is the same as for gastritis. The diagnosis is never certain until the jaundice appears. The patient must be prepared for a course of treatment lasting from three to six weeks. The more rigorous the early treatment the more likely the attack is to be mild and to run its course in a few weeks. Attention to small details is very important. Bed rest is rarely necessary, but it is advisable for the patient to remain at home for the first two or three

days. After that he may attend to his usual duties, avoiding, however, every physical strain and limiting his exertions. The object of treatment is to nourish the patient as well as possible while establishing the most favorable conditions for the subsidence of the catarrhal duodenitis or papillitis.

Every patient during the first two or three weeks will lose from 5 to 10 pounds body weight, and no particular attention need be paid to this fact. We expect him also to complain of a certain lassitude and weakness. No constitutional treatment is required at this stage, and none is in any way effective. Care in diet and the use of proper laxatives bring about an uncomplicated recovery in most cases.

All drastic purgatives or cholagogue cathartics are entirely out of place. They do harm by congesting and irritating the already swollen mucous membrane of the papilla and the duodenum.

For many years, following the lead of Eichhorst, I have used by preference the compound licorice powder, ordering at first 1 teaspoonful stirred in water night and morning. After the first few days the morning dose can be omitted. The licorice powder seems to be especially well tolerated in this condition and to act without griping. Many clinicians prefer the saline purgatives, especially sodium phosphate, sodium sulphate, or Carlsbad salts. These are administered in hot water twenty to thirty minutes before breakfast; the dose may be repeated one-half hour before the evening meal. Calomel in minute doses is recommended by many clinicians at the outset of the disease. In my opinion it will sometimes do harm at this stage. Especially when there is bilious vomiting small doses of calomel often aggravate the symptoms. After the first few days, or at the end of the first week, minute doses of calomel, gr. 1/10 to 1/20, may be given every hour for one or two days, often with great benefit. Large enemata of physiological salt solution, which have proved of great value in chronic jaundice, are very useful; but they may usually be dispensed with in the acute disease. If enemata are used the water may be quite warm or even cool. Cold colon irrigations must be avoided, as they may produce collapse. The Lyon's method of flushing the duodenum with a 33 per cent solution of magnesium sulphate introduced through the duodenal bucket will be referred to later (see page 725). It is probable that equally good results are achieved by the methods just mentioned.

The diet during the first few days should consist of milk diluted with limewater or alkaline mineral water, such as vichy. Cereals are well tolerated, especially rice, farina, and the wheat foods. Excess of cream must be avoided. Patients usually have a distaste for fats, and these should be excluded from the dietary. Milk toast is an excellent article of food for the first few days. Toast, zwieback, and Holland rusk are permitted. After the acute symptoms have passed away, Irish potatoes, creamed asparagus tips, and string beans may be added to the list.

Toward the end of the second week the patient may indulge in the softer meats, such as stewed chicken, sweetbreads, and scraped beef. Throughout the course of this disease he must absolutely avoid all alcoholic beverages, greasy or fried foods, acid drinks, and fruits. Friedenwald has shown that catarrhal jaundice is accompanied by an increased secretion of HCl, the hyperchlorhydria keeping pace with the jaundice. This fact explains the necessity for the dietetic restrictions just mentioned. Carelessness in diet is almost sure to be followed by increased discomfort, and convalescence may be delayed for weeks, or the catarrhal condition may even become chronic. It is not wise to allow an unlimited diet too early. We should wait until the last trace of jaundice has entirely disappeared before permitting the patients to eat stewed fruits (preferably prunes or apples), or to indulge in the coarser vegetables, such as corn, beets, spinach, carrots, peas.

The itching of the skin rarely becomes very annoying in the acute form of catarrhal jaundice. Lotions containing 2 or 2½ per cent carbolic acid are useful. Warm baths are moderately helpful. I have frequently seen good results from the following lotion recommended by Dr. Howard Morrow:

℞	Liquor carbonic detergens	12.0
	Liquor plumbi subacetatis	16.0
	Glycerin	16.0
	Aq. dest. qs. ad	240.0

Hypodermics of pilocarpin, gr. 1/4 to 1/6 (0.015 to 0.01 gm.), are said to be useful in obstinate cases. Osler recommends McCall Anderson's dusting powder. This is composed of starch, 30 parts, camphor, 6 parts, and zinc oxid, 15 parts.

After the subsidence of the acute symptoms dilute nitromuriatic acid in 15-drop doses after meals is frequently beneficial. The modus operandi is doubtful; the clinical fact is sure. During convalescence tinct. of nux vomica, tinct. of gentian, and other stomachics may be used. As a rule, the patients do as well without them as with them. Mild exercise, fresh air, and the avoidance of all nervous strain must be insisted upon until the health is completely restored. The convalescence is rarely interrupted if care in diet is exercised. No special after treatment is required.[1]

Chronic Catarrhal and Relapsing Jaundice.—The clinician is sometimes confronted with cases of obstinate or recurring jaundice in which the diagnosis may for a long time be uncertain. An acute catarrh of the bile passages may become chronic through neglect, and in those addicted to

[1] A 10 per cent salve of menthol in lanolin frequently gives great relief. In some patients menthol dissolved in alcohol, 10 per cent, seems more efficacious. At times less menthol should be used; in very nervous subjects the sensation of cold produced by menthol is followed by increased nervousness.—Editor.

alcohol one attack may follow another with only short intervals. Prolonged catarrhal jaundice may simulate an impacted common duct stone or may be a symptom of Hanot's disease (hypertrophic biliary cirrhosis). On the other hand, chronic jaundice may be dependent on organic lesions, such as stricture of the common duct, the pressure of tumors or portal glands, chronic pancreatitis, etc. Treatment must always be instituted before a diagnosis can be made, as the latter will often be based upon the results of the former. When medical treatment fails, operative interference will usually be called for. Hypertrophic biliary cirrhosis can occasionally be cured by continued drainage of the gall-bladder, though this operation is frequently without avail.

The medical treatment includes:

1. Gastric lavage.
2. Colon irrigations.
3. Restriction of the diet.
4. The use of proper drugs.

Gastric lavage is indicated in every case complicated with gastric catarrh. The stomach should be washed out every morning before breakfast or one-half hour before the noon or evening meal. Lavage should be continued so long as mucus or food appears in the wash water. There is no advantage in adding soda, antiseptics, or any drugs to the water, which should be fairly hot to the touch. As the patient improves, the lavage should take place every second, then every third, day, and finally it should be dispensed with altogether.

Many clinicians have noted the good effect of lavage in various inflammatory conditions of the bile passages and the gall-bladder. It acts in various ways, principally by ridding the stomach of mucus and of germs adhering to the walls; and probably also by bringing about a healthier circulation in the walls of the stomach and bowel.

Colon irrigations are more useful than gastric lavage. Large quantities of warm 0.5 per cent salt solution (2 or 3 liters) should be employed daily, either in the late afternoon or at bedtime. Part of the water thus used is absorbed and flushes out the portal circulation. It also removes much toxic material from the bowel, thus sparing the liver cells. The colon irrigations should be continued until the jaundice has completely disappeared, and until the constitutional symptoms (itching, mental depression, and irritability) have subsided.

The dietetic rules are, in the main, the same as are employed in other hepatic derangements. Greasy foods are absolutely forbidden, though fresh butter may be used in small quantities. Cream is not to be taken. The cruder and acid vegetables, such as cabbage, tomatoes, turnips, celery, cauliflower, rhubarb, radishes, navy beans, must all be omitted. All raw fruits are injurious, and even stewed fruits are better dispensed with in

the great majority of cases. Condiments and all alcoholic beverages must be absolutely avoided. Buttermilk is usually not well borne. Many patients do better without eggs in any form. There is no objection to a moderate quantity of meat once daily. Sweet milk is well tolerated, also cereals, potatoes, and the simpler green vegetables. Light puddings and simple cakes, custards, and gelatin preparations are all suitable. The patient should take his three regular meals without extra lunches.

Drugs are useful in combating this disease. The most important is calomel, given after all the inflammatory symptoms have entirely disappeared. It should be given in minute doses ranging from gr. 1/10 to gr. 1/40 (0.006 to 0.0015 gm.) every hour, and its use may be extended over many days, or, if need be, weeks, with intermissions. A good routine plan is to order on alternate days gr. 1/20 (0.003 gm.) to be taken hourly for ten doses. The day following a saline is administered before breakfast, preferably a mixture of Epsom and Glauber salts with sodium bicarbonate. The calomel is to be begun immediately after breakfast and continued hourly until the ten doses are taken. Patients tolerate calomel well if given in this manner, and show no disturbance of the digestion or of their general well-being. The tongue becomes clearer, the sense of epigastric oppression rapidly diminishes, and the liver becomes markedly reduced in size after the first, second, or third day. If the bowels become too active under this treatment, or if there are signs of irritation, such as the appearance of mucus in the stools, the calomel should be stopped and the salines may be continued once or twice daily, or it may be advisable to rely altogether on the colon irrigations until the signs of irritability are gone. Other "cholagogue" cathartics may also be used, but always in small doses. Large doses almost always do much more harm than good, and may increase the catarrhal swelling.

It is not wise to persist indefinitely with medical treatment. One must be guided by the condition of the patient. Most surgeons consider two or three months' duration of jaundice an indication for operation. If the catarrhal nature of the jaundice can be ruled out an operation is indicated much sooner. Many internists have seen jaundice which has persisted for a longer period clear up eventually without operative interference. Steady deepening of the jaundice is an indication for immediate surgical relief. Before an operation is undertaken it is wise to administer calcium chlorid, 2.0 gm. (gr. xxx), three times daily for five or six days in order to avoid hemorrhages. The intravenous use of calcium chlorid once daily for three days is more effective.

Syphilitic Disease of the Liver.—Jaundice may accompany the secondary manifestations of syphilis. If not treated adequately it tends to become chronic. The treatment is that of syphilis, not that of catarrhal jaundice. Inunctions or the internal or hypodermic administration of mercury causes the jaundice to disappear in the large majority of cases.

Salvarsan is the remedy of choice.[2] The treatment must be prolonged or relapses are apt to occur. The ordinary treatment of catarrhal jaundice is entirely without avail.

Tertiary syphilitic manifestations take the form of a diffuse interstitial hepatitis or of gummatous deposits. In both instances the liver is markedly enlarged. Later on bands of cicatricial tissue may form and the liver may contract or may present characteristic constrictions. The latter forms are not amenable to treatment, but the earlier stages usually yield to active antisyphilitic measures. Billings gives a good review of this subject. He concludes that mercury is the best specific medication. It may be given by mouth, by inunction, by deep intramuscular injection, or intravenously. Billings prefers the intramuscular injections, using salicylate of mercury in doses of 1 gr. (0.06 gm.) daily or on alternate days. Fifteen to twenty-five injections are given. This course is followed by the iodid of potassium, which Billings thinks is especially valuable in gummatous disease. Small doses may give satisfactory results or the dose may have to be increased to from 300 to 400 gr. (20.0 to 30.0 gm.) daily. It is best to give the iodid after the mercurial injections.

A second course of these injections should be given in three or four months. Billings speaks highly of the value of arsphenamin, but doubts that it will give better results than mercury and the iodids. Rolleston points to the necessity in many cases of using antisyphilitic measures persistently for many weeks before results are achieved. Gummata have occasionally been successfully resected; suppurating gummata have been scraped out with marked benefit to the patient. Medical treatment should follow these operations.

Congenital syphilis of the liver must be treated along the usual lines. Rolleston gives the following directions: Mercury with chalk may be given in doses of ½ gr. (0.03 gm.) twice daily to infants under two months, in doses of 1 gr. (0.06 gm.) to older children. Mercurial inunction is a more satisfactory method. At the beginning 15 gr. (1.0 gm.) of mercurial ointment should be used every day; it is rubbed on with flannel into the axilla, over the liver, over the spleen, a fresh location being chosen each day. This treatment should be carried out daily for three months, in the fourth month the treatment being intermitted for a week at a time, and in the fifth month for two weeks. In the second year of treatment mercurial inunction should be performed during one month out of three and a small dose of iodid of potassium given. In the third year the dose of the iodid may be increased, and in the fourth year the mercurial treatment may be dropped while the iodid is continued.

During recent years neo-arsphenamin has been used with good results. In very young infants it should be given intravenously. The veins of the

[2] Wile and others have recently called attention to the danger of too aggressive arsphenamine treatment in hepatic syphilis.—Editor.

scalp or the sinus longitudinalis are favorable sites. Wechselmann's epifascial method is suitable for older children between the age of two and seven years. Regarding the dosage, the initial dose of neo-arsphenamin should always be small, about 0.05 gm. being suitable for a newborn infant. At one month of age 0.1 gm. may be given; at six months 0.2 gm.; and gradually up to 0.35 gm. at 18 months.

Cholecystitis and Cholelithiasis

To treat the diseases of the gall-bladder intelligently it is necessary to have a clear idea of the relationship existing between cholecystitis and cholelithiasis. In health the bile is practically always sterile. Cholecystitis is due to an infection. The most frequently encountered germs in infected bile are colon bacilli, typhoid bacilli, staphylococci, pneumococci, the influenza bacillus and streptococci. These germs gain entrance to the gall-bladder through the arterial circulation or by means of the portal circulation or possibly through an ascending infection from the duodenum. Infection by streptococci may be limited to the wall of the gall-bladder, the contained bile being sterile. Colon bacilli and typhoid bacilli may be found in the center of gall-stones, even in cases where no living germs are encountered in the bile. It is evident, therefore, that the bacterial content of the bile obtained either at an operation or with the duodenal bucket is no criterion of the condition of the gall-bladder itself. Catarrhal cholecystitis is a catarrhal inflammation of the lining membrane of the gall-bladder due to infection. The continued presence of these germs in the gall-bladder is very apt to be followed by the formation of gall-stones. This is especially true if catarrhal cholecystitis is present. The following facts must be clearly borne in mind:

1. The first attack of catarrhal cholecystitis is often overlooked, being mild in character and transient. It is apt to be followed by recurrences.
2. The severe attacks are quite characteristic. They are accompanied by slight fever, epigastric pain, tenderness in the region of the gall-bladder, and gastric symptoms lasting several days.
3. Either the mild or the severer attacks may result in a chronic catarrh which leads to the formation of gall-stones.
4. Catarrhal cholecystitis may possibly be chronic from the beginning and insidious in its onset; in these rare cases gall-stones may form without a preceding history of pain or digestive disturbances.
5. The symptoms from which the patient suffers are due in a large proportion of cases to the cholecystitis and may be entirely independent of the stones.
6. Only in a minority of cases is the clinical history dominated by the stones themselves.

Treatment of Acute Catarrhal Cholecystitis.—The simpler attacks of acute cholecystitis are treated like cases of acute gastritis or acute indigestion, with which conditions they are often confounded. If the stomach contains food at the onset of the attack, vomiting should be induced by administering large quantities of lukewarm water. The addition of salt or mustard to the water has no advantage. If vomiting is delayed, the patient may hasten it by pushing his finger as far back on the tongue as possible. When vomiting is not readily induced in this way the patient should resolutely hold his finger in place until the vomiting ensues. The use of the stomach tube is rarely, if ever, indicated. One act of vomiting does not usually empty the stomach. It is best for the patient to repeat the process one or more times until the water returns clear. Complete rest is then necessary. If tenderness in the gall-bladder region exists, warm wet compresses should be applied. The patient should usually abstain from all food for at least eight to ten hours, though a cup of hot tea and dry toast can often be taken to advantage one-half to one hour after cessation of the vomiting. Continued retching can best be combated by an ice-bag over the epigastrium, preferably applied directly to the skin for a few hours.

Nothing is more valuable than from 3 to 5 drops of pure chloroform swallowed with a teaspoonful of shaved ice every half hour! This remedy is also valuable to combat a sense of epigastric pressure which is often felt for many hours. When retching is violent, aromatic spirits of ammonia, compound spirits of ether, and similar drugs *often do more harm than good.* Equal parts of the spirits of chloroform and camphor in from 5 to 10-drop doses on cracked ice is an efficient remedy.

Morphin in small doses given hypodermically is not usually necessary, but it should be administered without hesitation if pain and vomiting are excessive.

Efforts at feeding should not be begun until the nausea and pain have entirely subsided. Hot tea is usually well tolerated. Simple gruels (barley, oatmeal) make an acceptable beginning; toast or bread and butter may soon be added.

After the second day the usual diet may gradually be resumed. If swelling of the gall-bladder has been recognized during the attack, and if tenderness of the gall-bladder region remains after the attack, the patient is confronted with the probability of relapses and with the possibility of the formation of gall-stones.

Under these circumstances it is clear that the treatment of the patient should not cease with the passing of the attack. It is highly probable that careful and prolonged after treatment will prevent a recurrence of the attacks, and may prevent the formation of gall-stones.

Not nearly enough attention has been paid to this point. The initial attack of cholecystitis is a critical epoch in the patient's life. If the

presence of cholecystitis is not recognized, or if the condition is neglected after the attack, there is every chance that the gall-bladder infection may become chronic and that gall-stones will eventually form. There is reason to believe that months are required for the actual formation of stones. It has been pretty well demonstrated that continued infection is required for this formation. Active and persistent treatment is, therefore, indicated for some weeks or months following every attack of cholecystitis. It is possible that urotropin is valuable in inhibiting the growth of bacteria in the bile. I have seen at least one striking case of typhoid infection of the gall-bladder subside quickly after the administration of urotropin in doses of 5 gr. every three hours. After even a mild attack of cholecystitis the patient should be subjected to the same regulations as if gall-stones were definitely known to be present. These regulations will be described in detail further on.

Treatment of an Attack of Gall-stone Colic.—The acute pain during the attack is to be combated by the hypodermic use of morphin. Many drugs are mentioned in this connection, and the list is copied from book to book. In actual practice morphin in doses of ¼ to ½ gr. (0.015 to 0.03 gm.) is the one drug indicated. In robust individuals, when the pain is excruciating, an initial dose of ½ gr. (0.03 gm.) is not too much, but the dose must be increased with caution. It is easy to induce morphin poisoning if too large doses are used. In old patients, or when the pain is less intense, it is wiser to begin with ¼-gr. doses (0.015 gm.),[3] but this may be repeated in fifteen or twenty minutes if required. Obstinate attacks may necessitate a third dose. The physician should never leave the patient until the pain is entirely overcome and the complete effect of the morphin can be estimated. This rule is the more imperative if large doses have been given. At the very onset of the pain the inhalation of chloroform is advised until the morphin has had time to act, but this will be rarely feasible or desirable.

When, for one reason or another, morphin cannot be administered hypodermically, some opium preparation may be taken by the mouth. Paregoric in teaspoonful doses, best given in a wineglass of hot water, repeated two or three times at short intervals, may be tried. Laudanum or the deodorized tincture of opium may be added to the dose, so that each teaspoonful of paregoric contains 10 minims (0.6 gm.) of the deodorized tincture. Administration of remedies by the mouth is exceedingly unreliable because absorption from the stomach does not take place, and gastric peristalsis is either inhibited or is reversed. Caution against poisoning the patient must be observed. Hot applications over the epigastrium and right hypochondrium are useful. Wet applications are better than dry. There is no value in excessive heat and the zeal of attendants to scald or burn the skin has nothing to recommend it. Thick

[3] Or less.—Editor.

flannel or a folded towel wrung out of very warm water answers every purpose. An oiled silk covering is useful.

When the patient awakes from the morphin sleep he may experience considerable pain in the epigastrium or in the gall-bladder region. Recurrence of the severe paroxysm is always possible. It is often wise to continue the use of morphin by mouth for from twenty-four to thirty-six hours after the initial paroxysm. The following formula given by Whitla I have used in scores of cases and have found it almost invariably well tolerated:

℞	Morphinæ sulphatis	gr. i	(0.06 gm.)
	Bismuthi subcarbonatis	gr. xlv	(3.0 gm.)
	Acidi hydrocyanici diluti	gtt. viii	(0.5 c.c.)
	Mucilaginis acaciæ	℥vi	(24.0 gm.)
	Aquæ chloroformi q. s. ad	℥ii	(60.0 c.c.)

Sig. Shake well. One teaspoonful every one to three hours if required. (As the sediment in this prescription tends to pack tightly on the bottom of the bottle, it is advisable to keep the bottle lying horizontally.)

During the first twenty-four hours after the attack it is usually advisable for the patient to abstain from all food and drink. If tenderness is present in the gall-bladder region large warm Priessnitz compresses are very useful in allaying inflammation. The compresses should be continued day and night until all tenderness and swelling have absolutely subsided.

All purgative medicines are strongly contra-indicated during the first twenty-four hours. It is not unusual to see the administration of purgatives followed by marked exacerbations. As in all inflammatory processes, the chief indication is local rest, and this is best attained by starvation and functional inactivity. Even enemata should be avoided for at least from twenty-four to thirty-six hours after the onset of the attack. At the end of this period a simple soapsuds enema may be given and the patient may begin to take food. Oatmeal and barley gruels are usually well tolerated; hot tea and unbuttered toast are easily taken; milk diluted with limewater may be given. Milk toast and broths free of fat can soon be added.

In a few days the patient may be taking fair quantities of food, though, as a rule, a light diet is to be preferred. All acids, fruits, and coarse vegetables must be forbidden the first few weeks. Even eggs act treacherously in some cases. It is advisable to avoid eggs in all cases in which bilious vomiting has been a feature.

Treatment of Chronic Cholecystitis and Cholelithiasis.—There is no medical treatment for gall-stones as such. By medical means we cannot effect any important change in the gall-stones themselves. As an important corollary to this statement, it must be added that gall-stones as such do not usually produce symptoms. The history of patients who have gall-

stones is usually determined by the inflammatory changes which persist in the gall-bladder or which recur or flare up from time to time.

Exceptions to these generalizations are found in those cases in which the gall-bladder is packed with and overdistended by a large number of stones, and in those rare instances in which, in the absence of inflammatory attacks, the stones become lodged in the excretory ducts of the liver.

It should be clearly understood that the object of medical treatment is to reduce the gall-bladder and its contents to a harmless condition. We no longer endeavor or expect to get rid of the stones by medical treatment, although this is sometimes incidentally accomplished. The aim of medical treatment is accomplished if active inflammatory processes subside, and if the gall-bladder is made to functionate without distress. The object of treatment, in other words, is to render the gall-stones latent and to transform the patient from a "gall-stone sufferer" to a "gall-stone carrier." In addition it is often necessary to treat those reflex functional disturbances and symptoms which an irritated or inflamed gall-bladder sets up in other parts of the digestive system, particularly the stomach.

The treatment of chronic cholecystitis and cholelithiasis includes local measures, physical rest, dietetic régime, and the use of mineral waters and drugs.

Gall-Bladder Drainage.—In September, 1919, B. B. Vincent Lyon published a preliminary report of a new method for the diagnosis and treatment of diseases of the gall-bladder and biliary ducts. This was followed in due time by a series of eight other papers containing a large amount of polemic, experimental and clinical material. The method was received with widespread interest and has given rise to a large literature, most of it dealing with the diagnostic value of the procedure and only a small part of it devoted to its therapeutic aspects. In March and April, 1922, Lyon critically reviewed all the literature up to that date and gave a complete bibliography to which the reader is referred. Lyon's work was based on an observation of S. J. Meltzer who, in experimenting with magnesium sulphate, had observed that the application of a 25 per cent solution of that salt to the duodenal mucosa was followed by a completely local relaxation of the intestinal wall. Lyon found that when he introduced solutions of magnesium sulphate of varying strengths and in varying quantities directly into the duodenum by means of the duodenal bucket, the procedure was followed within from two to fifteen minutes by a gushing of bile into the duodenum, and this bile could readily be regained by aspiration. Upon this observation Lyon built an elaborate process for the recovery of bile for diagnostic purposes from the common duct, from the gall-bladder and from the higher bile ducts; and he likewise utilized the method for the topical treatment of the diseases of the bile ducts and gall-bladder. Lyon is of the opinion that Meltzer's law of contrary innervation applies to the biliary apparatus and that stimulation

of the duodenal mucosa with magnesium sulphate and other excitants causes a relaxation of the sphincter of the papilla of Vater and coincidentally a contraction of the gall-bladder itself, leading to the expulsion of its contents. To this process systematically used Lyon gave the name of "non-surgical biliary tract drainage," and by this name it is now generally known in medical literature.

Lyon first employed this method in the treatment of *catarrhal jaundice* and thought that he greatly reduced the duration of the disease by this process. After the duodenal bucket was in place, he aspirated the duodenal contents for study, and then introduced 50 to 100 c.c. of 25-per cent solution of magnesium sulphate. This solution was allowed to remain a few minutes and was then aspirated by means of a low pressure vacuum bottle. In 2 of the 7 cases thus treated the plug of mucus in the papilla was removed at the first treatment and bile was obtained from the ducts and the bladder. In none of the cases were more than three daily treatments required to produce this result. Following the biliary drainage the duodenum was disinfected with potassium permanganate or silver nitrate solutions of a strength of 1 : 10,000. From 100 to 200 c.c. of these solutions were used at a time and an attempt was made to regain the fluids by suction three to five minutes after their application. No harm ensued if the fluids escaped recapture. The drainage was repeated every second to fourth day until a cure was effected.

Lyon later used his method for a great variety of conditions. He thinks it is indicated in early infections of the gall-bladder, catarrh of that organ, and what he calls atony of the gall-bladder. When surgical procedures are contra-indicated by serious disease of the kidneys or the vital organs, gall-bladder drainage can be employed as a temporary expedient for reducing toxemia and clearing up the local conditions as well as possible. After operations on the biliary system the method is recommended to drain the residual infection left in the ducts or liver. Lyon concludes after a large experience with many kinds of seriously sick patients that many have been cured by his methods and that only a comparatively few have not been greatly benefited. When the gall-bladder is a focus of systemic infection, vaccines can be prepared from the bacteria recovered from the gall-bladder and thereby patients can be greatly helped or cured.

In many cases gall-bladder drainage should be repeated frequently in the same patient. At each treatment three or four douchings with the magnesium sulphate solutions should be given. Every four or five days the treatment should be repeated, not only until the patient is clinically cured but until the cytological and bacteriological conditions of the obtained bile have returned to normal. This cannot always be accomplished. In Lyon's record of 73 cured cases, 47 of the patients still yielded pathological bile specimens on direct examination.

Technic of Gall-Bladder Drainage.—When the method is employed for diagnostic purposes strict attention must be paid to asepsis of the nasal passages, the mouth, and throat, the teeth and the gums. In therapeutic work these precautions are not necessary. The treatment can be carried out in a hospital, in the patient's home or at the physician's office. The patient presents himself in the morning after a twelve-hour fast. The duodenal bucket is swallowed slowly. After the tube has entered the stomach, the patient lies down on the right side (the right lateral Sims' position with slightly elevated hips is preferred) and *very slowly* swallows an additional 20 cm. of tubing, up to 75 or 80 cm. from the teeth. *The patient should take not less than twenty minutes to swallow the last 20 cm. of tubing.* This prevents coiling within the stomach and offers the most favorable opportunity for the tube to enter the duodenum. The entrance into the duodenum requires anywhere from fifteen minutes to one hour; occasionally much longer. During this time the patient should read or be otherwise diverted. The duodenum is then douched with 50 to 100 c.c. of warm 33 per cent solution of magnesium sulphate. After three to five minutes this solution is aspirated. Soon bile begins to appear and this may be allowed to siphon itself off until the flow ceases. The process can be repeated two or even three times within the hour.

This is not the place to review in detail the many objections which have been made to the Lyon's method both as a diagnostic and a therapeutic procedure. Discussing it purely from the therapeutic side, certain known facts should be borne in mind. The musculature of the gall-bladder is very feeble. Its power of contraction is scarcely able to overcome the normal secretion pressure of the bile. To speak of atony of the gall-bladder is a misuse of terms and concepts. It is not probable that the gall-bladder ever contracts sufficiently to expel a large part of its contents at one time. Rather, the flow of bile is a steady dribble when the pressure in the common duct and the duodenum is less than that higher up. To speak of drainage of the gall-bladder is to employ a figure of speech not based on definitely ascertained facts. The only known cholagogues are the bile salts themselves. The products of gastric digestion physiologically stimulate the flow of bile upon entering the duodenum. It is doubtful that magnesium sulphate exercises any specific influence on the papilla or even upon the flow of bile.

It is also difficult to see in what way drugs or chemicals, even if they did stimulate a flow of bile, would be beneficial in ridding the bile ducts or the gall-bladder of an infection. In the pathological conditions under discussion bile is constantly flowing into the duodenum. Non-surgical drainage of the bile passages is constantly taking place in health and disease unless there is an actual obstruction to the flow of bile, and the Lyon's method cannot remove stones or other obstructing agents. Observation has taught us that many diseased gall-bladders harbor streptococci

in their walls, the bile itself being sterile. Certainly these cases cannot be cured by introducing magnesium sulphate into the duodenum for five minutes every third or fifth day. We know that the concentration of the bile and the readiness of its flow can be influenced by various factors—food, bile salts, sugars, starvation, etc. (see Introductory Note). The clinical value of salines in modifying pathological processes in the biliary system under proper hygienic conditions is fully attested by years of observation and experience. It is probable that attention to hygienic and dietary details in connection with the appropriate use of salines and other drugs can accomplish everything that we can hope to accomplish by purely medical treatment. From the reports so far published it is not clear that the Lyon's method of so-called non-surgical biliary drainage has brought about any results which had not been achieved previously by methods long since in vogue.

Local Measures.—Local measures are indicated during the exacerbations of inflammation. They are of no obvious use in the absence of physical signs. When, however, there is a discoverable enlargement of the gall-bladder, or any degree of sensitiveness in the gall-bladder region, or when there is a tender Riedel's lobe, external applications are of undoubted value. As a general rule, it may be stated that the thoroughness and duration of external treatment depend entirely upon the local signs. Very warm Priessnitz compresses are to be preferred to all other forms of application, except in acute purulent exacerbations, when an ice-bag should be given the preference.

During an acute inflammatory attack the Priessnitz compresses, covering the whole upper half of the abdomen, should be applied continuously during the twenty-four hours. As the local tenderness becomes less marked the compresses may be omitted during the nights; in the later stages of the treatment the patient lies down with the compresses two hours in the forenoon and two hours in the afternoon, and this treatment is continued until the physical signs have completely disappeared. Persistence of the physical signs for several weeks under this treatment is an absolute indication for operative interference. The exact time of operation will depend on the judgment of the physician.

Among the local measures may be included colon irrigations with physiological salt solution. Nearly all pathological processes within the liver are alleviated more or less by this means, and irrigations should be performed daily during the subacute inflammatory stage. When the patient is able to take large quantities of hot salines the colon flushing may be discontinued.

Rest.—The value of physical rest in the treatment of cholelithiasis has not been sufficiently emphasized. There is no doubt that violent exertions tend to bring on attacks of colic and retard recovery. Horseback-riding, automobile tours, and all athletic sports must be prohibited for

months following any active symptoms. R. Kolisch says that all Carlsbad physicians *without exception* value rest in the treatment of gall-stones. Hence it comes that severe attacks in Carlsbad, where 10,000 patients are treated annually, are a great rarity. Even during an active Carlsbad course of treatment exercise is not a necessity. After patients leave Carlsbad they must have no abdominal massage, no gymnastic exercises, and no athletic sports for one year. Under these restrictions, says Kolisch, the vast majority of Carlsbad visitors remain well.

Diet.—There is much divergence of opinion regarding the proper diet for cholelithiasis. During the acute inflammatory stage the diet should be limited to cereal soups, gruels, milk and limewater, bread, and toast. The simpler vegetables may soon be added, especially Irish potatoes (baked or boiled) and the tips of creamed asparagus. In general terms it may be stated that all greasy and acid foods must be prohibited. Cholelithiasis is so often complicated by excretory abnormalities in the stomach, especially hyperchlorhydria, that the diet will often have to be determined by these outside factors. Personal idiosyncrasies must likewise be considered. This is especially true regarding eggs, which are well tolerated by many patients, but which are invariably followed by symptoms in others. Well-prepared meats are nearly always acceptable, except pork, bacon, goose, and sausage. Veal tongue or beef tongue, lobsters, and crabs must be avoided. Fatty soups should not be taken. All cereals are permissible, but macaroni and spaghetti should be prepared without cheese. Cheeses are usually well borne, but those which readily undergo acid fermentation, such as cottage cheese and New York creamery, are better omitted. Fresh butter is harmless. Hot breads are to be interdicted. Among the vegetables *well-prepared* peas, lima beans, spinach, corn, mushrooms, carrots, and asparagus are usually well tolerated. Tomatoes, cucumbers, beets, cabbage, cauliflower, radishes, sweet potatoes, and navy beans must be forbidden.

It is my experience that most patients who require treatment for gall-stones are better off without fruits of any kind. All fruits pass out of the stomach slowly, increase gastric acidity, and are irritating. Vinegar, mustard, horseradish, and other spices must be forbidden on the same grounds. Custards, light puddings, light cakes, and gelatins may be taken freely. Ice cream, ices, and sweets of all kinds are apt to cause trouble. Individual observation is here necessary.

Hot tea is a safe beverage; alkaline waters may be used with safety. Coffee, cider, lemonade, ginger ale, all highly charged waters, cocoa, and chocolate must be omitted. Alcoholic beverages of all kinds are harmful.

The above dietary suggestions do not apply in all cases. A certain proportion of patients have either complete achylia gastrica or subacidity. In these patients, acid fruits, vegetables, buttermilk or other acid beverages

are indicated and usually well tolerated, and the amount of albuminous food must be reduced.

It has been suggested that patients with gall-stones should eat frequently in order to prevent the bile from stagnating in the gall-bladder. In the fasting state the bile is stored up in the gall-bladder and the frequent occurrence of biliary colic at night has been explained by the distention of the organ, which occurs at that time. It is doubtful if this advice has any value in the average case. Patients with reflex gastric hypersecretion or hyperchlorhydria would, it is true, be benefited by frequent meals.

Mineral Waters and Drugs.—The value of the saline mineral waters in the treatment of cholelithiasis is universally recognized. The alkaline waters neutralize or reduce gastric acidity; they tend to reduce catarrhal processes in the stomach and in the upper intestines. They are also supposed to keep the bile thin and to stimulate its flow. The best time to administer the saline waters is from one-half to one hour before meals when the stomach is nearly or quite empty. Every experienced clinician has his own favorite formula. Some prefer the natural mineral waters of Carlsbad, Vichy, Neuenahr, Bedford, and consider treatment at the springs superior to home treatment. It is generally conceded that treatment away from home offers many advantages. Patients when visiting resorts for treatment gain the tonic effect of travel; they submit more willingly to the dietetic and other regulations; they are relieved of all duties and cares; and in general can devote themselves with more regularity to the use of the chosen waters. It is not generally believed that treatment at the source possesses any specific superiority over the home treatment beyond the advantages just named. Carlsbad is the most famous resort for gall-stone patients and most of the artificial formulæ are imitations of the Carlsbad waters.

In my opinion sulphate of sodium is the most valuable of all the salts usually employed, being far superior to the more generally used phosphate of sodium. A good formula is the following:

℞	Magnesiæ sulphatis	60.0 (℥ii)
	Sodii sulphatis	30.0 (℥i)
	Sodii bicarbonatis	10.0 (ʒiiss)
	M.	

Sig. One teaspoonful in a glassful of hot water one-half hour before breakfast and one hour before dinner and supper.

This formula is often too laxative in its effects and it may cause meteorism; it should be varied to meet various indications. In cases of marked hyperchlorhydria the amount of the bicarbonate can be increased as follows:

℞ Magnesiæ sulphatis 60.0 (℥ii)
Sodii sulphatis
Sodii bicarbonatis āā 20.0 (℥v)
Sig. One teaspoonful in hot water as directed.

Equal parts of the three salts constitute an acceptable formula. After the first two or three weeks of treatment the remedy should be omitted at noon; later the evening dose may be stopped, but the patient should continue the medicine in the morning for months or even years.

Billings recommends the following formula:

℞ Sodii salicylatis 10.0 (℥iiss)
Sodii phosphatis granulati 20.0 (℥v)
Sodii sulphatis exsiccati 60.0 (℥ii)
Sig. One teaspoonful in hot water one-half hour before meals, three or four times a day.

Forchheimer prefers the simple sodium phosphate given one, two, or three times daily. Occasionally patients cannot tolerate saline drugs without nausea or at least anorexia. In these cases pure hot water can be used. I would warn against excessively hot water or excessively large quantities of hot water, as I have seen many examples of gastric catarrh produced by indiscretions in this direction.

Before the pathology of cholelithiasis was so well understood the treatment was often directed to the solution or expulsion of the calculi. No one believes now that gall-stones within the gall-bladder can be dissolved by the administration of drugs. The use of strong purgatives and cholagogue drugs for the purpose of expelling the stones is not to be recommended. Large stones will not pass; smaller stones are apt to lodge in the excretory ducts, and even if some stones were expelled others would be likely to remain behind. As a rule, strong purgatives succeed only in irritating the inflamed bile passages without removing the stones. Milder cholagogues given over a long period of time, such as pure ox-bile, bile salts, salicylate of sodium, and various combinations of the above, are advised by many clinicians and in my opinion are often useful in preventing recurrent attacks. Tyson says:

"I have been in the habit of placing my patients between attacks on the succinate of sodium in doses of 5 gr. (0.3 gm.) three times daily, and it has so happened that I have seldom met a recurrence in one of these cases, although many of them passed out of my observation and may have had attacks without my knowledge."

Personally, I doubt the efficacy of the remedy.

Pure olive oil has a preëminent reputation with the laity and has proved useful in allaying many symptoms. It is best administered in

gradually increasing doses before meals and at bedtime. As much as a wineglassful may be taken at one time. Olive oil frequently removes the gastric symptoms of gall-stones, especially when these are dependent on hyperchlorhydria or reflex pylorospasm. Rolleston suggests the possibility of olive oil dissolving stones which are lodged in the papilla of Vater. During the use of olive oil small fatty concretions are often expelled in the feces and may be mistaken for gall-stones.

Treatment of Gall-stones in Transit.—Gall-stone colic may be followed by numerous complications. One or more stones may lodge in the neck of the cystic duct. In these cases the pains persist or recur with short intermissions, and accompanying the attacks of pain there is a gradual distention of the gall-bladder. Opiates are required at frequent intervals, and hot applications are only moderately successful in relieving the distress. Suppuration within the gall-bladder will be shown by a septic temperature and usually, though not always, by moderate or well-marked leukocytosis. Suppuration calls for surgical interference. It is proper to temporize if the symptoms are not life-threatening and if they show a tendency to recede. As in other intra-abdominal conditions, it is often better to wait until the acute inflammatory symptoms have subsided. Even in non-suppurative cases the indications become surgical as soon as more than a merely temporary obstruction in the cystic duct can be recognized.

When stones slip through the cystic duct and lodge in the common duct jaundice rapidly supervenes. During the first few days of the jaundice we are not able to tell if it is dependent on the presence of calculi or is due to catarrhal swelling of the mucosa. In fact, sometimes many weeks elapse before one can be sure on this point. It is therefore advisable to adopt a conservative course until the diagnosis is cleared up. The patient must stay in bed so long as there is evidence of inflammation of the gall-bladder or tenderness of the liver. During the first few days no strong purgatives must be permitted. The effort to drive supposititious stones through an inflamed duct by means of strong cholagogues must be condemned. The attempt is usually followed by increased pain and jaundice, that is, by increase of the local inflammation.

The diet must be carefully restricted, all greasy foods and acids being rigidly excluded. After the fourth or fifth day of jaundice colon irrigations with physiological salt solution should be practiced systematically, at least once in twenty-four hours. The saline purgatives in hot water may now be used, preferably those which contain sodium sulphate. Calomel may be often used to advantage if administered in minute doses, 1/20 to 1/10 gr. (0.003 to 0.006 gm.) every hour, until ten doses have been taken each day. In the absence of active inflammation no method is so good as this for reducing catarrhal swelling of the bile passages. Every morning a hot saline is given one-half hour before breakfast, and calomel is

begun immediately after breakfast. This plan may be continued daily, or on alternate days, for a long period, often with the most striking benefit.

The more chronic the obstruction the more we are justified in resorting to strong purgatives without fear of making bad matters worse. Personally I have rarely seen efforts to dislodge obstructing stones crowned with success, but innumerable cases have been recorded.

The drugs most frequently employed over a long period of time are olive oil, salicylate of sodium, gr. x (0.6 gm.) three times daily after meals, ether and turpentine in various mixtures, and tincture of chelodonium.

Just how long we should persevere with medical treatment depends upon the conditions present in each case. No absolute rules can apply. So long as the patient is in good condition and free of fever and pain we can afford to temporize. Continuous loss of weight, regular though slight rise of temperature in the afternoons, or pronounced debility may be considered more imperative indications for operative interference. The waiting period may extend ordinarily from one to three months. To prolong medical treatment beyond this period is to subject the patient to the danger of permanent damage of the liver structures, and increases the risk of the operation itself.

Rolleston advises persistent medical treatment even in the presence of recurrent attacks of fever and pain, but warns against allowing the patient to run down in health too far before resorting to an operation.

Respective Indications for Medical and Surgical Treatment of Cholecystitis and Cholelithiasis.—With a few exceptions, every gall-bladder disease begins as a medical case. In the great majority of instances the earliest symptoms are those of a catarrhal cholecystitis. These may be so mild that the true nature of the disease is overlooked, a diagnosis of simple "spoiled stomach" or "acute gastritis" being made. The severer cases are early recognized by the local signs and symptoms. Cholecystitis resembles appendicitis in this: that one attack predisposes to another, and also in the fact that a moderately severe attack may become latent or temporarily quiescent without, however, entirely clearing up. Cholecystitis differs from appendicitis in one very important particular, namely, the exacerbations are not nearly so likely unexpectedly to assume serious or even dangerous aspects. The main argument for the immediate operation in all cases of appendicitis rests upon the fact that it is impossible for the clinician to estimate with certainty the condition of the appendix, and this uncertainty makes the retention of a diseased appendix more dangerous than an operation for its removal.

Such is not the case in diseases of the gall-bladder. Unexpected surgical emergencies are here the exception, and the "tragic surprises" which accompany appendicitis are here so rare that they may be neglected in a practical discussion.

This radical difference in the clinical tendencies of the two diseases accounts for the fact that, whereas appendicitis has long been recognized as an essentially surgical disease, cholecystitis and cholelithiasis still occupy a fortified position in the *grenzgebiet* between medicine and surgery, with no lack of assailants and defenders in either camp.

There can be no question that a very large number of cases of mild catarrhal cholecystitis run a rapid course to complete and permanent recovery. That this is true of many moderately severe attacks I am led to believe by the careful observation of numerous cases over a long period of years. Even cases which are due to infection with the typhoid bacillus during or subsequent to an attack of typhoid fever usually end in complete recovery, and the numerous cases of so-called "typhoid carriers" who are in perfect health are a witness to this fact. Even so aggressive a surgeon as Deaver says:

"Typhoid cholecystitis rarely calls for operation. The majority progress favorably. I have followed too many cases to a sure convalescence without operation to believe that all cases arising in typhoid fever should be operated on."

I believe we are justified in classing all the moderate attacks of acute catarrhal cholecystitis as medical cases, and we may look for a permanent recovery in many instances under appropriate treatment. We may draw a further conclusion that the mere presence of recognizable inflammation in the gall-bladder is not per se an indication for surgical interference; we may go further and say that surgery of the gall-bladder in acute catarrhal cases without definite surgical indications is meddlesome and unnecessary surgery. The successful issue of surgical interference in these cases simply shows, as Sahli has said in another connection, that "many medically curable cases likewise recover when treated surgically."

It sometimes happens that an acute attack of cholecystitis is so severe that it becomes life-threatening. These attacks are ushered in by chills and fever and marked prostration, and soon give rise to localized or, in the worst cases, to diffuse peritonitis. In the majority of these cases there has been a preceding history pointing to chronic gall-bladder disease. When an ice-bag applied locally and supportive measures do not seem to fortify the patient against the progress of the disease, immediate surgical interference may be necessary. One cannot be guided by a white blood count in this emergency because some cases of purulent cholecystitis are not accompanied by marked leukocytosis. If it is possible to tide the patient over the acuter symptoms before operating, this should be done, but the most experienced judgment is required to estimate the chances correctly. It should be borne in mind that the number of cases requiring immediate surgical interference compared to the total number of inflammatory attacks is exceedingly small.

In estimating the indications for treatment in the more chronic forms of gall-bladder disease one meets with the greatest diversity of opinion. Some of the leading internists are radicals in advocating surgical interference in every case, while some of the most experienced surgeons refuse operation more frequently than they perform it.

Thus Frank Billings is quite positive in declaring in favor of surgery. He says:

"Gall-stone disease must be recognized as a surgical disease. The danger of cholangitis, hepatic abscess, perigastric adhesions, pancreatitis, etc., occurring as a result of gall-stones is so great that even the most conservative physician may well hesitate to take the responsibility of non-surgical treatment."

Surely an extreme view. On the other hand, Hans Kehr operated only on 1,300 out of 4,000 cases referred to him, and in his latest report he states that, "kein Chirurg wird mehr die frühzeitige Operation verlangen," that is "no surgeon will hereafter advocate an early operation," but should be satisfied if the cases are not sent to him altogether too late, that is, with neglected choledochus obstruction or septic complications. In the hands of the most experienced surgeons, says Kehr, almost the only cases which end fatally are cases of carcinoma or septic cholangitis. Kehr also believes that 80 per cent of all cases will become latent in time. In face of these facts he rejects for operation all cases except in the presence of the following indications: Absolute indications: chronic choledochus obstruction; acute and chronic empyema of the gall-bladder; perforation; cancer. Relative indications: chronic symptoms, which cause inability to work or to enjoy life.

We thus have the curious spectacle of an internist of wide experience pleading for surgical interference in all cases, and a surgeon with still wider experience advocating conservative medical treatment in most cases in the absence of vital surgical indications. It is impossible to quote all the opinions of the leading authorities on this subject. We must content ourselves with presenting the various arguments on which these opinions are based.

Arguments for Considering Chronic or Recurrent Gall-Bladder Disease a Surgical Disease and Operating in All Cases.—1. Operation affords the only means of a permanent anatomical as well as clinical cure. Medical treatment may relieve the symptoms; it cannot bring about an anatomical cure in the sense of dissipating chronic cholecystitis or removing gall-stones.

2. The early operation, that is, before complications have arisen, is safe. The mortality rate in the hands of experienced surgeons is nearly nil. Thus Kehr lost only 1 in the last 73 uncomplicated cases. The

Mayos' mortality in the same class of cases is only 0.5 per cent. The risk is increased by delay.

3. The early operation prevents complications, on the part of the gall-bladder itself (perforations, adhesions); on the part of the common bile duct (obstruction leading to cholangitis and septic infection); and on the part of the pancreas (pancreatitis, abscess). Lastly, it prevents the development of cancer.

These arguments may be summed up very briefly, thus: early operative interference is safe; it is sure; it prevents secondary and often pernicious complications.

Arguments for Considering Chronic or Recurrent Gall-Bladder Disease a Medical Disease in the Absence of Vital Indications.—1. In a very large proportion of cases chronic gall-bladder disease tends to a gradual clinical cure. In other words, gall-stones become latent, inflammation of the gall-bladder subsides or disappears, and the "gall-stone sufferer" becomes merely a "gall-stone carrier." Kehr estimates this proportion at 80 per cent. Goldammer makes the same estimate. Franz Fick has shown that, whereas autopsy records show a larger and larger prevalence of gall-stones at increasing ages, clinical records show the greatest prevalence of gall-bladder diseases between the ages of twenty-five and fifty. As patients grow older the gall-bladder gives them less trouble.

Every experienced clinician has observed many cases in which active gall-bladder symptoms have disappeared never to return.

2. The more serious complications of cholelithiasis are the result of neglect. It is true that careful living on the part of the patient and careful observation by the physician will prevent most, if not nearly all, of the life-threatening accidents connected with cholelithiasis.

3. The truly surgical complications do not, as a rule, arise suddenly, but, on the contrary, they usually give ample warning, so that there is plenty of time to operate when the indications call for an operation. For example, the severe forms of chronic cholecystitis are preceded by months or even years of local symptoms; only the neglect of obvious surgical indications permits the development of dangerous or fatal conditions. Cases which obstinately resist medical treatment and which, despite proper treatment, present persistent dyspeptic disturbances or attacks of recurrent jaundice may well be considered surgical cases. When life-threatening or fatal symptoms arise in this class of cases we may attribute the mortality to the inattention or indecision of the attending physician, but the theory of the propriety of medical treatment is unaffected.

This is especially well illustrated in cases of cancer of the gall-bladder. The occurrence of cancer of the gall-bladder as a well-known sequel of cholelithiasis is mentioned by nearly all surgeons as one of the prominent reasons for early operation. But it must be borne in mind that

cancer usually does not occur in cases which give a typical gall-stone history. The etiological relation between cancer and stones has not been absolutely proved. As Neusser has well said:

"The specter fear of the serious consequences of cholelithiasis, which the surgeons love to oppose to a conservative treatment, is much weakened by contrary considerations."

4. The results of surgical interference are not so uniformly good as the face returns of surgical statistics would indicate.

In the first place, the surgical mortality even in the uncomplicated cases is something. The most experienced surgeons lose from ½ to 1½ per cent in the simplest cases, and the mortality is undoubtedly greater in the average run of cases. We are in no position to judge of the post-operative morbidity, that is, of the per cent of patients in whom symptoms recur after even a successful operation. Recent statistics show a return of symptoms in from one-third to one-fourth of the cases after cholecystotomy. J. J. Buchanan estimates that after cholecystotomy only 70 per cent of the patients remain well. Graff and Weinert studied the end results in 124 cholecystectomized patients and found that only 73 per cent of these were actually cured. Every clinician is familiar enough with the persistent dyspepsia, the recurrent pains and the localized discomforts which many patients present after having had gall-stones removed. Add to these cases the small number of those who are harassed by adhesions, hernias, or fistulæ, and we readily see that operative interference is not always synonymous with clinical cure, and the clinical history does not always end with the departure of the patient from the hospital.

The arguments for the medical treatment of cholelithiasis may be briefly summed up thus: medical treatment results in a clinical cure in a large percentage of cases, possibly 80 per cent; the occurrence of serious complications may be foreseen, and may be forestalled by operative interference when called for.

After a thorough review of the whole subject the various indications for treatment may be summed up as follows:

Indications for Operative Interference.

1. Acute purulent cholecystitis threatening life.
2. Perforation of the gall-bladder.
3. Gangrene of the gall-bladder.
4. Chronic distention or thickening of the gall-bladder. In the words of Quenu, "hydrops calls for an operation, empyema demands it."
5. Persistent dyspeptic symptoms, especially when accompanied by physical signs of a diseased gall-bladder.
6. Chronic obstruction of the common duct extending over a period of one to three months.

7. Chills and fever in the course of the disease with signs of enlargement of the liver, local tenderness, or jaundice.

8. The presence of symptoms which seriously interfere with the work of the individual or his ability to enjoy life. The occupation of the patient, his means, and his environment play a rôle in this decision.

Indications for Medical Treatment.

1. Simple catarrhal cholecystitis.

2. The early attacks of biliary colic, before the ability of medical treatment to render the stones latent has been thoroughly tested.

3. Cases of cholelithiasis in which the attacks are infrequent and not accompanied by obvious complications.

4. Cases of cholelithiasis with predominating gastric symptoms due to hyperchlorhydria and without marked local signs.

5. Cases with serious complications on the part of the kidneys, heart, or blood-vessels which would render surgical interference dangerous.

DISEASES OF THE LIVER

Cirrhosis of the Liver

(*Portal or Laennec's Cirrhosis*)

For practical purposes we may divide the clinical history of cirrhosis of the liver into three stages:

1. The stage of development, during which the presence of the disease may be suspected but cannot be proved. Enlargement of the liver may or may not be demonstrable.

2. The active stage, during which ascites is the predominating symptom.

3. The terminal stage, presenting various phases of toxemia.

Treatment of the Developmental Stage.—We are justified in suspecting the oncoming of cirrhosis in patients who have been addicted to the stronger alcoholic beverages and who, with little or no warning, have copious hemorrhages from the stomach or bowels, or who, in the absence of hemorrhage, present a more or less constant enlargement of the liver, combined with the symptoms of gastro-intestinal catarrh and marked nervousness, and who void a scanty quantity of highly colored urine, which has a high specific gravity, but which contains a moderate or subnormal quantity of urea. These patients usually have a muddy complexion, which is sometimes even subicteric in character; they also become

reduced in weight and strength. The presence of alimentary levulosuria increases the probability of the presence of cirrhosis.

The treatment during this stage may succeed in delaying or preventing the progress of the disease. The objects of the treatment are:

1. To remove all the etiological factors.
2. To remedy the gastro-intestinal symptoms.
3. To inaugurate a system of diet and medication which has been clinically shown to be favorable in diseases of the liver.

The use of alcoholic beverages must be absolutely and permanently prohibited. Drugs must be avoided which contain a large percentage of alcohol. During the advanced stages of cirrhosis absolute abstinence from alcoholics may be attended with more harm than good, but in the early stages total abstinence must be insisted upon. The patient must omit all highly spiced foods containing mustard, pepper, horseradish, or other condiments.

The gastro-intestinal symptoms usually require special treatment. Alcoholic gastritis is frequently present. Gastric lavage is of marked advantage in this condition. The stomach may be washed out every morning before breakfast, several quarts of warm water being used. The addition of drugs to the wash water has no advantage. Instead of the lavage, the patient may drink large quantities of hot water, from ½ pint to a pint, one-half to one hour before breakfast. When constipation is present a teaspoonful of the natural or artificial Carlsbad salts may be dissolved in the water. Many patients are benefited by taking a teaspoonful of Carlsbad salt or similar preparation one-half hour before breakfast and one hour before dinner and supper. A good formula is equal parts of magnesium sulphate, sodium sulphate, and sodium bicarbonate. If purging is too active the dose may be reduced one-half, or the salts may be administered in the morning, the hot water alone being taken in the forenoon and afternoon. Hot water is not always well tolerated, but may increase an existing gastritis. When well borne it is often markedly beneficial, carrying off the gastric mucus, "flushing out" the liver, and stimulating the circulation in the stomach. In cases of hypoacidity dilute hydrochloric acid or the nitrohydrochloric acid may be given with advantage. Fifteen or 20 drops well diluted and taken before or after meals sometimes relieve the sense of fullness in the stomach and reduce the belching. Vomiting, if present, is usually relieved by the measures just mentioned. Gastric sedatives, such as subnitrate of bismuth, dilute hydrocyanic acid, are often useful. The bitter tonics, gentian, nux vomica, condurango, are relatively ineffectual. The digestive ferments never yield more than merely temporary results.

Diet.—The diet of patients in the early stages of cirrhosis of the liver should be carefully controlled. Unfortunately the science of chem-

ical physiology has not advanced sufficiently to give us rational guidance. Empirically we have learned that all greasy foods and most acid foods are not well tolerated. All stimulants, including coffee, must be avoided. A pure milk diet is theoretically advisable, but is rarely practical. Few patients remain well nourished on a milk diet, and few can continue it without disgust or marked dyspeptic disturbances for any length of time. Milk makes few demands on the digestive organs, is a good diuretic, does not lend itself to harmful putrefactive changes in the colon, and is, therefore, invaluable where it can be well tolerated. It should form the chief article of nourishment so long as it is easily and pleasantly taken and so long as it is digested. Very often the milk can be modified to advantage.

The addition of bicarbonate of sodium or limewater reduces the tendency to flatulence and dyspepsia. The addition of barley gruel or other cereal diluents is rarely palatable to adults for any length of time. The various preparations of fermented milk are all valuable, but usually they do not possess any advantage over the ordinary milk. Skimming the milk renders it more digestible.

Practically a pure milk diet is rarely successful for any length of time. It is of the utmost importance that the strength of the patient be not sacrificed to any theoretic considerations whatsoever. Therefore, a mixed diet is preferable in nearly all cases. All the cereals are appropriate. Well-prepared bread is a desirable addition. Good butter may be taken freely. The use of vegetables and fruits must be governed by the condition of the stomach and bowels. The more acid fruits, such as oranges, grapefruit, peaches, plums, must be avoided. The coarser vegetables, such as cabbage, kale, tomatoes, and radishes, must be forbidden.

Much diversity of opinion exists regarding the desirability of meat. My own experience leads me to believe that well-prepared meats, beef, chicken, sweetbreads, lamb, roast veal, are valuable and harmless additions to the dietary and may be taken once daily without harm. The more easily digested fishes are also acceptable. The very fatty fishes, as well as pork, bacon, tongue, goose, lobster, and shrimps, should not be taken. Eggs are well digested by some patients and upset others. It is necessary to individualize. Critical observation and a not too close adherence to theoretic considerations are recommended. In patients with advanced atrophic gastritis meats and eggs should be prohibited; buttermilk, fruits and vegetables should form the main diet.

Drugs.—The use of drugs has a distinct place in the treatment of the early stages. Formerly it was believed that malaria played a rôle in the development of cirrhosis and quinin was often given, but without benefit. It is now known that true hepatic cirrhosis is not due to malaria. The value of iodid of potassium is problematic. In cases occurring in syphilitic patients the iodid should be pushed to the point of tolerance.

In non-syphilitic cases I have never seen any good results from the

use of the iodids. On the contrary, patients are often made much worse by pushing the remedy at the expense of the digestion and the appetite. I am convinced that the drug is useless or even harmful in the ordinary cases, and it is not indicated unless there is a suspicion of syphilis. In the absence of a positive Wassermann or Noguchi test the iodids should not be given. Rolleston, Stadelmann, and others think that iodid of potassium should be given a trial, even if syphilis is not known to be present. A few authors (Forchheimer, Eichhorst) believe that good results have been obtained in the early stages of non-syphilitic cirrhosis by the long-continued use of moderate doses of the iodid of potassium, but the large majority of observers are of a different opinion.

Calomel is a more useful drug. Its systematic use was formerly much lauded by many German clinicians. It is undoubtedly of great value in the hypertrophic form of cirrhosis (Hanot's disease), and in all cases of alcoholic cirrhosis in which there is an associated catarrh of the bile passages.

There is a wide variation in the dosage. Large doses sometimes exert a markedly beneficial influence. Two-tenths gm. (3 gr.) may be given three times daily for a period of three days, these doses to be repeated after an interval of several days. Calomel can advantageously be given in minute doses for its effect both on the liver and the intestinal contents. Rolleston recommends 0.006 to 0.003 gm. (gr. 1/10 to 1/20) given three times daily. I have frequently given calomel 0.003 gm. (gr. 1/20) hourly for days at a time with markedly beneficial effects. An occasional dose of a saline purgative before breakfast is of advantage during the calomel treatment. We must avoid reducing the strength of our patients by strong purgatives, and any treatment which deranges the digestion or lowers the vitality of the patient does more harm than good.

Treatment at a foreign or native watering resort is desirable in the early stages if the patient has the necessary leisure and money. The spa treatment has well-recognized advantages. Travel has a tonic effect. Patients are relieved of their daily cares and duties. They have nothing to distract their mind from the systematic habits required at the various resorts. They are more obedient to dietetic rules. The gastric and intestinal functions are stimulated to heightened activity by the hot mineral waters. The flushing of the stomach and intestines reduces the possibility of auto-intoxication, and catarrhal processes in the bile ducts, stomach, and small intestines are relieved. Especially useful are Carlsbad, Vichy, Homburg, Kissingen, Harrogate, French Lick, and Bedford Springs.

Treatment after the Appearance of Ascites.—Hale White takes a most gloomy view concerning the outlook for patients in whom ascites has supervened. "There appears no doubt," he says, "that, when ascites is not due to simple chronic peritonitis or tubercular peritonitis, its supervention in cirrhosis means that the patient will die within two or three

months." This conclusion has so many exceptions that we are justified in rejecting so pessimistic an attitude toward our patients, and there is no doubt that scrupulous attention to details will often be followed by more favorable results, especially in private practice. Certain it is that well-established cirrhosis cannot be cured anatomically; nevertheless, cases are recorded in which apparent cirrhosis with ascites has been followed by a clinical recovery for many years. Subsequent autopsies in some of these cases have shown that the patients had cirrhosis which had become latent. It is likewise true that many patients dying of other diseases are found postmortem to have had cirrhosis of the liver.

The treatment of ascites has two aims:

1. The removal of the fluid.
2. The prevention of its reaccumulation.

Hale White sees no advantage in the removal of the fluid unless the breathing and the action of the heart are impaired. The modern tendency, however, is to withdraw the fluid as soon as the patient is seriously embarrassed by its presence. It is surely preferable to perform early paracentesis than to exhaust the strength of the patient by vigorous purgation, which is almost invariably futile.

Diuretics do little toward removing accumulated fluid, though they are of some advantage in preventing its reaccumulation. The dangers of paracentesis when properly performed are few. Debove and Castaigne, in a brief but brilliant monograph, call attention to the precautions which should be thrown about this apparently trivial operation. They, in common with most French authorities, consider the point of election to be the junction of the outer with the middle third of a line drawn from the umbilicus to the anterior superior spine of the ilium. The median line a few inches above the symphysis pubis is also a suitable place. The patient should empty his bladder before the puncture. A small trocar should be used so that the escape of fluid is not too rapid. Strict antiseptic precautions should be taken. The best method of procedure is the following:

If the lateral point is chosen the patient lies in bed; for the median puncture the patient may be seated in a rocking-chair, which is tilted backward. The abdomen is thoroughly scrubbed with soap and water. The skin at the site of puncture is painted with tincture of iodin. It is then sprayed with ethyl chlorid. A small incision is made through the skin with a small knife and the trocar is then plunged directly into the peritoneal cavity. The fluid should be permitted to escape slowly. If the patient is in fair condition all the fluid should be removed. It is convenient to attach a rubber tube to the cannula in order to conduct the fluid to a basin on the floor. After the fluid has all escaped the cannula is removed and a silk suture closes the wound. This is

then covered with a piece of aseptic gauze. Instead of closing the wound with a stitch it may be painted over with collodion; the suture is preferable. A cannula may be left in place for a few days in order to retard the accumulation of fluid. It soon ceases to drain and its retention in place has few advantages.

After the fluid has been removed or even during its removal it is generally recommended to fasten a bandage about the abdomen and to draw it as tight as the patient can endure with comfort. A cat-o'-nine-tails bandage is best for this purpose. The bandage is supposed to prevent faintness on the part of the patient from overfilling of the abdominal vessels, and even to forestall hemorrhages from the same cause. During the past few years I have usually dispensed with this precaution altogether and without regret.

After removal of the fluid one should not overlook the opportunity of immediately palpating accurately the liver and spleen. Many details connected with these organs can then be made out which are obscured by the presence of fluid. Debove and Castaigne discuss in detail the dangers connected with tapping. They classify them into two groups, called the immediate and the remote complications. The immediate complications include hemorrhages from the wall of the abdomen; hemorrhages from the gastro-intestinal canal; and cardiopulmonary disturbances. Hemorrhage from the wall of the abdomen is due to wounding of the epigastric artery. The blood may escape externally, may infiltrate the abdominal wall, or finally may be poured into the abdominal cavity, with fatal results. Rapid collapse after paracentesis should suggest this possibility and lead to a search for the hemorrhage.

Hemorrhages from the digestive tube are due to rapid decompression. They usually cease spontaneously, but may prove fatal. Hence the necessity of the compressing bandage after the puncture.

The cardiovascular disturbances may occur during the paracentesis or shortly thereafter. Intense dyspnea and rapid dilatation of the heart may occur, leading to a fatal collapse. This complication must be guarded against by using proper cardiac stimulants before the operation in all weak patients. Digitalis is especially valuable. Hypodermoclysis of 250 c.c. physiological salt solution may be given one hour before the operation, and may be repeated after twelve hours. In very debilitated subjects it is advisable to remove only a few liters of the ascitic fluid, enough to prevent the mechanical embarrassment caused by the fluid. The remote complications are two in number and only gradually follow the removal of the fluid. The first is called by the French writers "l'anémie séreuse," that is, exhaustion of the blood-serum; the second is a deep jaundice, the so-called icterus gravis, which supervenes a few days after paracentesis. Both of these complications are prevented by observing the precautions already mentioned.

How Can Reaccumulation of the Fluid Be Delayed or Prevented?—*A milk diet* is strongly advocated by many French clinicians. Lancereau in particular considers it an absolute condition of success. The milk diet acts in two ways: (1) by sparing the liver cells; and (2) by stimulating copious diuresis. Many cases are on record in which the rigid milk diet prolonged over many weeks was followed by a disappearance of the ascites and a complete clinical cure. Approximately 3 liters should be administered daily, but the quantity will vary with each individual. *The salt-free diet* was first used in the treatment of the ascites of cirrhosis in 1903 by Achard and Paisseau. It has been tried with varying success in hundreds of cases since that date. All observers agree that the absorption of fluid from the peritoneal cavity under the influence of the salt-free diet is not nearly so rapid as the disappearance of edema of the legs in cases of nephritis or heart disease. There is no doubt, however, that ascites has been made to disappear by withholding all salt from the dietary.

An interesting summary of observations was published by Henri Guilhaume. Among his conclusions are the following:

1. Under the influence of a salt-free diet ascitic fluid is absorbed less readily in cases of cirrhosis of the liver than in cases of Bright's disease or cardiac insufficiency.
2. The therapeutic results are superior to those obtained by a milk diet.
3. The salt-free diet should be tried in cases of cirrhosis as rigidly as the endurance and taste of the patient will permit.

Sir Clifford Allbutt describes a sensible method of using the salt-free diet:

"At first only the salt on the table is forbidden. The next step is to reduce the salt in the dishes, the bread and butter, etc., so that in four or five days more all salt is rigorously excluded. The total exclusion is tolerable for another four or five days, when a little salt may be added to the cooked food or to the bread, and so gradually a return made not to ordinary quantities of salt, but to so much as may be really necessary."

Many French clinicians encourage the use of calcium salts in connection with the salt-free diet. Ten to 15 gm. of calcium chlorid (preferably the anhydrous salt) should be given daily for five or six days.

Organotherapy has been tried in cases of cirrhosis. Usually the uncooked liver of hogs is taken in daily doses of about 150.0 gm. (5 oz.). Successful cases were reported in 1896 by Vidal and by Gilbert and Carnot. Mouras reported 7 cases in which the ascites was cured by organotherapy and collected other cases. Debove and Castaigne have not seen glowing results from this treatment, and call attention to the danger of infecting the patient with tubercle if the raw liver is employed. Various

drugs have been recommended to delay the accumulation of fluid. Diuretics are preferable to cathartics because they are less exhausting to the patient. Hale White thinks highly of copaiba resin in doses of 15 gr. (1.0 gm.). The pill known as Baillie's or Addison's pill, composed of 1 gr. each (0.06 gm.) of powdered digitalis leaves, squill, and blue mass, is very popular and often efficient. Musser recommends apocynum, of which the tincture can be given in doses of 15 to 30 minims (1.0 to 2.0 c.c.) three times daily, or the fluid extract in doses of 10 minims (0.6 c.c.) three times daily. Calomel in minute doses is often useful. Diuretin is not beneficial. Iodid of potassium is without avail.

Purgatives if pushed to extremes do more harm than good. In moderate doses they do not seem to prevent the accumulation of fluid. Jalap is probably the most beneficial.

In 1909 Eichhorst spoke in the highest terms of the value of cream of tartar, not only to prevent the accumulation of fluid, but also to cause its rapid absorption. Eichhorst's formula is as follows:

℞

Decocti althaeæ	180.0	(℥vi)
Potassii bitartratis	15.0	(ʒiiiss)
Syrupi simplicis	20.0	(ʒv)

Sig.—Shake well. One tablespoonful every two hours.

Jüsgen reports the results of using Eichhorst's remedy in the St. George Hospital in Hamburg. His conclusions are very favorable. The mild cases showed rapid improvement; even in severe cases with marked ascites and edema the ascites quickly disappeared. Nephritis delays, but does not prevent, favorable results so long as the heart is not seriously damaged. Dock reports a case which showed marked improvement under the use of compound jalap powder which contains cream of tartar.

Reducing the quantity of fluid ingested may temporarily limit the accumulation of fluid, but has so many objectionable features that it cannot be recommended.

The surgical treatment of the ascites of cirrhosis was originated independently by Talma and Morison. It was based on an effort to aid nature in establishing a collateral circulation between the portal and the systemic venous system. F. P. Weber thus describes the theory of the operation:

"Cases of hepatic cirrhosis might perhaps be roughly divided into the two following groups:

"A. Patients who for some reason (for instance, the presence of old perihepatitis and perisplenitis and extensive spontaneous omental adhesions) have the collateral venous circulation well established, and do not readily develop ascites, but are especially liable to hematemesis from

dilated esophageal or gastric veins. The liver is generally decidedly enlarged in this group of cases.

"B. Patients with a poor collateral venous circulation who develop ascites early. The main object of omentopexy and peritoneal drainage should be to convert patients of Class B into patients of Class A."

The technic of the original Talma operation or the Talma-Morison operation must be sought for in textbooks on surgery. Numerous modifications have been devised by other surgeons.

It is difficult to estimate the value of surgical interference. The publication of many successful cases resulting in good health for many years encourages operative treatment. Nevertheless, a large majority of the patients operated on either received no benefit at all or had their lives shortened by the operation. Undoubtedly hundreds if not thousands of unfavorable cases have never been reported. Dock suggests that the facts be laid before the patient himself. Many a patient would brave the danger of the operation in the hope of a possible cure. Rolleston says:

"When medical treatment and a course of iodid have not benefited a case of ascites, which is thought to be due to either syphilis or cirrhosis, the question of operative interference should be considered."

The earlier the operation is performed the better the chances of permanent relief. To operate in a late stage means almost inevitably to meet with failure. An excellent and very complete review of the surgical procedures for both the biliary and portal cirrhosis will be found in the *Annals of Surgery,* 1922, pages 449 to 458.

Treatment of the Terminal Stage.—Of 34 fatal cases in the clinic of Professor Spillman and Bernheim in Nancy, 7 died of spontaneous hemorrhage, 1 of hemorrhage after paracentesis; 5 died of icterus gravis; 3 of uremia, 6 of tuberculosis, 5 of bronchopneumonia, 1 each of heart failure and infection, and 2 of simple peritonitis.

When the disease runs its course the final stages are often marked by delirium and coma. These symptoms may be of renal, intestinal, or hepatic origin. Hemorrhages may occur at any stage in the disease; in fact, hematemesis is frequently one of the earliest symptoms. The treatment of the hematemesis is the same as in cases of gastric ulcer. Absolute rest, absolute abstinence from food or drink, the external application of ice, and the use of morphin hypodermically comprise the routine treatment. The patient must lie flat on his back at least for three or four days; an ice-bag should be placed on the epigastrium. If the patient is shocked or restless, nothing is so useful as morphin given hypodermically in doses of gr. ¼ to gr. ⅛ (0.015 to 0.008 gm.) repeated every three to six hours if required. Hypodermoclysis may be needed in severe cases. The patient

should not be permitted to suck ice or sip water. Hemostatic agents by mouth or hypodermically are of little or no avail. Horse serum, coagulose, and human blood-serum are often useful. Transfusion of blood may be life-saving. Calcium chlorid in dram (4.0 gm.) doses may be given by the rectum. After the hemorrhage has ceased at least twenty-four hours should elapse before feeding either by mouth or by rectum is begun. Rectal injections of 8 oz. (250 c.c.) of salt solution every six hours answer every requirement and are preferable to nutrient enemata. After forty-eight hours iced milk mixed with equal portions of limewater should be given per os, beginning with 2 oz. every two hours. No absolute rules can be given; larger or smaller quantities seem to be tolerated equally well. One must be guided by the symptoms. Patients often live many years after the initial hemorrhage. The after treatment is given in detail above. When hemorrhage from the stomach or bowels occurs in the terminal stage of cirrhosis, the end of the patient is not far off. Turpentine enemata are recommended by Rolleston for severe attacks of melena without hemetemesis. Hemorrhage from other mucous membranes should be treated locally when possible (epistaxis, hemorrhoids, etc.); multiple hemorrhages usually indicate advanced hepatic insufficiency and signify an early end.

The delirium and coma must be treated in a palliative manner. Strenuous efforts to prolong life to the utmost by means of packs, transfusions, etc., are not in place. When the outlook is hopeless it becomes the duty of the physician to prevent suffering, rather than to prolong life.

Prolapse of the Liver or Hepatoptosis

Mild grades of liver displacement are not infrequent. Total prolapse is much rarer. It occurs principally in women over forty who have borne several children and who present various symptoms of neurasthenia. It is commonly associated with geneal visceroptosis and almost always results from a weakening of the intra-abdominal ligaments and the abdominal wall. It must be understood that complete ptosis of the liver usually involves a double rotation of the liver, in addition to the dropping of the organ. The liver rotates on a transverse axis, so that the diaphragmatic portion moves anteriorly, bringing the anterior surface into greater contact with the anterior abdominal wall. The under surface of the liver turns also to the left, the convexity to the right. The liver thus becomes easily palpable, moves easily under the hands, drops when the patient stands, and can be pushed back into place when the patient lies down.

The treatment must fulfill three indications:

To Support the Prolapsed Organ.—In the milder grades this can be accomplished by any well-fitting abdominal supporter which, like all proper abdominal bandages, must bring most pressure to bear on the lower half of

the abdomen. In the severer cases we must resort to strapping with adhesive plaster or to the use of specially designed corsets. Strapping with adhesive plaster has the obvious disadvantage of being only a temporary appliance; the strapping must be frequently renewed; it tends to irritate the skin and cannot be compared in permanent comfort with a proper corset. The requisites for a good corset are thus excellently summarized by W. Hale White:

"It should have a firm grip on the ilia, be loose at the upper part, and be so made that by lacing it from below upward considerable pressure is brought to bear on the lower part of the abdomen; it should be laced up when the patient, in the erect posture, drawing a deep inspiration, thus raises the ribs and at the same time contracts the abdominal muscles as much as possible."

To Increase the Tone of the Abdominal Walls.—This can be accomplished by abdominal massage, by electricity, and by gymnastic exercises. The usual exercises for increasing the power of the abdominal muscles are these:

The patient lies on his back, and keeping the legs stiff raises and lowers the upper half of the body six to ten times. Or, lying flat, he alternately bends and straightens out the legs with the body held rigid. Deep breathing exercises are also of value.

To Increase the State of Nutrition of the Patient.—This relieves hepatic congestion, and tones up the muscular system. Detailed instructions are not necessary. The principles of dieting will be discussed under Enteroptosis. The use of cholagogue cathartics is invaluable and general tonics are usually indicated. When palliative measures fail to relieve the symptoms sufficiently resort may be had to surgical procedures. This is only exceptionally necessary. Gerard Marchant was the first to fix the liver by suturing it to the costal margin in 1891. Since that date various other methods of suturing and attaching the liver have been successfully employed.

Abscess of the Liver

Multiple abscesses of the liver of pyemic origin and suppurative pylephlebitis are practically always fatal and are not amenable to medical or surgical treatment. The only hope of successful treatment in the future is along the lines of serum treatment. All we can do at present is to combat the general pyemia.

The solitary abscess of dysentery, the traumatic abscess, and the suppuration by extension from a purulent gall-bladder can all be successfully treated by the surgeon. It is probable that the more general adoption of the ipecac treatment in cases of dysentery will somewhat limit the incidence of hepatic abscess, which complicates dysentery in from 15 per cent

to 30 per cent of all but the acute cases. The chances of recovery are increased by an early diagnosis. Diagnostic puncture of the liver should, therefore, be practiced "on suspicion" and is a harmless procedure when properly carried out. A few years ago a young man from Florida was under my care for intermittent fever and liver pains. He had had dysentery, but had no discoverable amebæ in the stools and no local signs. Owing to the persistence of symptoms and the exclusion of other possible foci, liver puncture was freely performed, and revealed a deep-seated abscess, which was opened and drained by Dr. H. T. Whitacre with perfect results.

George F. Johnson says that "surgical treatment must be prompt and bold and radical. No measure will succeed which does not completely evacuate the abscess cavity and allow free drainage. This can be done with precision and safety only by incision. Aspiration, puncture with trocar, direct puncture with scalpel, opening by caustics, or the thermocautery are uncertain, insufficient, dangerous, and unsurgical, and are mentioned only to be condemned."

When an abscess points or when its location can easily be determined on exposure of the liver it is often best to perform the operation in two stages. There is considerable room for difference of opinion as to the advisability of operating after rupture of the abscess into the lung. The best practice seems to be to postpone operation until the patient's health can be built up by tonics, good feeding, and sea air. Rupture of the abscess into the colon or externally is usually followed by spontaneous recovery. Rupture into the peritoneal cavity, the pleura, the pericardium, or elsewhere calls for immediate surgical interference.

Tumors and Cysts of the Liver

The simple cysts and benign tumors of the liver are usually pathological curiosities and have comparatively little clinical interest. A growing tumor should always arouse suspicion of syphilis and should be treated accordingly with large doses of iodids or mercury (see Syphilis of the Liver). Early surgical interference will probably result in the saving of some lives in cases of primary carcinoma, especially of the gall-bladder. Resection of the diseased areas is carried out successfully by modern methods. Actinomycosis of the liver should be treated by large doses of the iodids. Hydatid disease is curable surgically in the large majority of cases. C. MacLaurin gives a record of 420 cases of hydatid disease treated in the Royal Prince Albert Hospital in Sydney. During the past five years the operative mortality was only 1 to 2 per cent. "The only cases which now die," says MacLaurin, "are some of those which were ruptured and a few which have suppurated." The ultimate outcome in this disease, however, is always doubtful. Recurrence is common and

the peritoneum frequently becomes involved. This complication is usually fatal. The operation of choice is the excision of the mother cyst. By preference the posterior transcostal route is selected when possible.

Cancer of the liver, when primary, nearly always runs a very rapid course, so that only a few months elapse between the onset and the fatal termination. Not all cases require opiates, but morphin should be given without stint when pain is a prominent symptom. The treatment of secondary carcinoma is purely symptomatic. I am of the opinion that much suffering can be spared the victims of gastro-intestinal cancers by reducing the diet to the simplest possible rations, excluding, so far as is possible, all albuminous foods. Barley and oatmeal soups, and gruels should be the basis of the diet. Opiates, when required, should be given. Many a patient, however, has his total suffering increased by the too early and careless use of morphin. In general terms, we may say that, when patients have an incurable malignant disease, our efforts should be directed not to prolonging life, but to making it tolerable.

REFERENCES

Achard and Paisseau. Bull. et mém. Soc. med. d. hôp., 1165, 1903.
Allbutt. Musser and Kelly, Pract. Treat., ii, 96, 1911.
Billings. Diseases of the Digestive Tract, Mod. Clin. Med., 505, 1906.
——— Journ. Am. Med. Ass., Nov. 8, 1911.
Buchanan, J. J. Tr. Am. Surg. Ass., xxxiii, 316, 1915.
Collombier. Thèse de Nancy, 1908.
Deaver. Brooklyn Med. Journ., 6, 1905.
Debove and Castaigne. La Cirrhose de Laennec, Consult. méd. Franç., No. 6, 1910.
Dock. Tr. Am. Med. Ass., 168, 1909.
Eichhorst. Med. Klin., No. 11, 1909.
Elsner. N. Y. Med. Journ., 913, 1910.
Fick. Erfolg d. Karlsbader Kur und Chir. Behand. d. Gallensteinleidens, 1903.
Frazer. The Effect of Magnesium Sulphate on the Secretion of Bile, Journ. Am. Med. Ass., Nov. 4, 1922.
Friedenwald. Med. News, July 22, 1905.
Graff and Weinert. Beitr. z. klin. Chir., xcii, 339, 1914.
Guilhaume. Le Régime Dechlorure dans les Ascites Cirrhotiques, 1908.
Gilbert and Carnot. Soc. Biol., Nov. 21, 1896.
Johnson. Ann. Surg., 424, 1897.
Kehr. München. med. Wchnschr., 1986, 1910.
Kolisch. Med. Klin., 530, 1910.
Lancereau. Bull. Acad. de méd., 1887.

Lyon, B. B. Vincent. Journ. Am. Med. Ass., lxxiii, 980, 1919.
——— A Reply to Certain Antagonistic Criticism of Non-Surgical Biliary-Tract Drainage, N. Y. Med. Journ., March 1, April 19, 1922.
MacLaurin. Brit. Med. Journ., Oct. 1, 1910.
Meltzer, S. J. Am. Journ. Med. Sc., 469, April, 1917.
Morrow. Ref. Handbook Med. Sc., vi, 772.
Mouras. Thèse de Paris, 1910.
Rolleston. Diseases of the Liver.
Tyson. Pract. Med., 5th ed., 1909.
Weber. Proc. Roy. Soc. Med., Clinical Section, 80, 1909-1910.
White. Common Affections of the Liver, 1908.
Wynter. Minor Medicine, 3, 1910.

CHAPTER XXXIII

DISEASES OF THE PANCREAS

WILDER TILESTON

General Considerations.—In 1898 Oser wrote: "We are rarely in a position to make a correct diagnosis of pancreatic disease, and therefore can seldom employ a rational mode of treatment." The work of recent years, however, has greatly enriched our knowledge of the pancreas and its diseases in all directions, so that to-day we are often able to diagnosticate correctly, and cure or alleviate diseases of this interesting gland.

As is well known, the pancreas is a gland possessing both an internal and an external secretion. It is with the latter that we are concerned here, as the internal secretion is dealt with in the chapter on Diabetes. The work of Wohlgemuth and of Bickel has shown that the amount of the pancreatic secretion can be influenced to a considerable extent by diet and drugs. Thus bouillon, alcohol, sodium chlorid, hydrochloric acid, and pilocarpin all increase the secretion, while alkalis, atropin, and opium diminish it. The amount secreted is least on a fat diet, somewhat greater on one of protein, and largest on a carbohydrate diet. The concentration of the ferments, however, varies widely under different conditions, and no definite laws for man have been established yet. The pancreas secretes very little except under the administration of food by the mouth, so that in rectal feeding and starvation we possess ways of temporarily setting the gland at rest.

Secretin injected subcutaneously causes an active secretion of pancreatic juice in animals, and this secretion can be inhibited by the injection of adrenalin, as shown by Pemberton and Sweet. These facts, however, have not proved of value in practical therapeutics.

DIGESTIVE ACTION OF THE PANCREATIC JUICE

The external secretion of the pancreas contains three ferments: proteolytic, diastatic, and fat-splitting. The proteolytic ferment is secreted in an inactive form, trypsinogen, which is activated to trypsin by entero-

kinase. Trypsin carries on gastric digestion of protein, splitting peptones and albumoses into amino-acids. The pancreatic diastase completes the work of the salivary ferment. The lipase, working in combination with the bile, splits fats into fatty acids and glycerin, and in some way facilitates their absorption.

The pancreatic juice is essential for the complete utilization of fat and protein, as has been shown by the experimental work of Hess and Pratt, and by absorption experiments in man performed by Brugsch, Tileston and others. The fat loss in cases of exclusion of pancreatic juice without jaundice averages 55 per cent of the intake, and may reach as high as 83 per cent; the loss of nitrogen is less, averaging 39 per cent. If jaundice is present, the fat loss is higher, ranging from 58 to 87 per cent. In obstruction of the bile duct alone, the fat loss is considerably less, from 30 to 45 per cent.

The digestion of starch is well carried out in the absence of pancreatic juice by the other diastatic ferments.

Recognition of Decreased Pancreatic Function.—Total absence of the pancreatic juice from the intestine may be recognized by simple methods without the use of elaborate tests, by the presence of bulky fatty stools, with microscopic neutral fat and undigested muscle fibers in large amounts. "Butter-stools," that is, stools with masses of fat visible to the naked eye which congeal on cooling, are by no means rare if looked for carefully, and are pathognomic of pancreatic disease. They were present in 4 out of 6 cases examined by the writer. The administration of 100 gm. of fat in the form of olive oil may facilitate the appearance of this sign.

In obstructive jaundice without interference with the pancreatic secretion, the stools are fatty but not bulky, and microscopically the fat is in the form of fatty acid needles rather than droplets of neutral fat, and "butter-stools" and creatorrhea (numerous undigested muscle fibers) are never met with. Creatorrhea is indicative of pancreatic disease, in the absence of diarrhea. (The stools in the absence of pancreatic juice are usually frequent, but not watery.)

Glycosuria is not uncommon in pancreatic disease, and when present has great diagnostic value. It is often transitory, so that it may be overlooked unless frequent examinations are made. A lowered sugar tolerance, though somewhat less reliable than glycosuria, is suggestive.

Functional Tests of the Pancreas.—In regard to the functional tests, it may be said that none of them is absolutely reliable, except in cases where the diagnosis is possible without them. From the results of several of them, however, a conclusion is often possible. They will be considered in the order of their importance.

Examination of Duodenal Contents.—This is probably the most reliable method, and absence of ferments, especially of trypsin, indicates with certainty disease of the pancreas. Simple diminution of the ferment

content, however, is of less importance, owing to the wide variation of the figures in normal persons.

Examination of the Stool for Ferments.—This examination is less reliable than that of the duodenal contents, but may be helpful, and is much less troublesome. The Gross casein test for trypsin has yielded good results in the writer's hands, but only in a qualitative sense, to indicate the presence or absence of pancreatic secretion. Opinions are conflicting with regard to the determination of diastase in the feces, many writers regarding it as without value, while T. R. Brown, using a special technic, has obtained apparently trustworthy results.

Test for Urinary Diastase.—Here again authorities are not agreed, Wallis regarding the test as of great value while McClure and Pratt come to the conclusion that it is of little use in the diagnosis of a pancreatic disease, unless greatly increased values (more than 500 units) are found, which is seldom the case.

The *Schmidt nucleus test,* and its modification by Kashiwado, possess some diagnostic value when carefully performed, with controls on healthy persons. It is usually positive when no pancreatic juice is present, but has been found positive also in a number of cases where there was no definite pancreatic disease.

The *Löwi adrenalin test* is not of much help, being often negative in pancreatic disease, and positive in the absence of such disease.

The Sahli capsule, the Winternitz sajodin and the Cammidge tests are too untrustworthy to repay the time consumed in performing them.

Opotherapy.—Where the pancreatic juice is deficient, it has been shown that the administration of raw pancreas or of pancreatic extract often increases materially the absorption of both fat and protein. Raw pancreas is somewhat more effective than the extracts, but is harder to procure, and usually soon becomes distasteful to the patient. If gastric achylia is present, any active preparation will do. Otherwise pankreon, a combination of pancreatic extract and tannic acid which is not affected by the hydrochloric acid of the gastric juice, may be employed. Or an alkaline medium for the pancreatic extract may be insured by giving large amounts of calcium carbonate (1 to 3 gm.). Large doses are necessary, from 4 to 12 tablets of pankreon (0.25 gm. each) or 1 to 3 gm. of pancreatin after each meal.

Surgical Treatment of the Pancreas.—Experience has demonstrated that the pancreas may be attacked quite freely, extensive resections may be performed, free incisions may be made, or small pieces may be removed for examination without danger, provided that injury to important adjacent structures (splenic artery and vein, pancreaticoduodenal and middle colic arteries, inferior vena cava, etc.) is avoided, adequate drainage is supplied, and the peritoneum is protected from the corrosive action of the pancreatic juice.

Routes of Approach to the Pancreas.—Various methods of exposing the pancreas for the purposes of operation have been devised. They may be divided into transperitoneal and extraperitoneal routes. Of the former there are three: (1) through the gastrohepatic omentum, useful only in cysts presenting above the stomach, and in marked ptosis of the stomach; (2) through the gastrocolic omentum, the usual route when exposure of the whole gland is desired; and (3) through the transverse mesocolon, for cysts presenting below the colon, and for exposure of the tail of the pancreas. The extraperitoneal routes are the lateral abdominal one of Bardenheuer and the lumbar. The former is said to give a good exposure of the body and tail of the pancreas, while the latter is useful only in the drainage of cysts and abscesses of the organ.

The best works to consult on diseases of the pancreas are those of Opie, Pratt, Robson and Cammidge, and Heiberg. Oser's monograph in *Nothnagel's Encyclopedia,* though out of date, contains much valuable information.

PANCREATIC HYPOCHYLIA (ACHYLIA)

In 1906, Schmidt described a condition which he termed "functional pancreatic achylia," in which there were diarrhea and evidence of deficiency of the pancreatic secretion, associated with achylia gastrica or other gastric disturbances. Since then his observations have been confirmed by Mayer and others, although Brugsch remains very skeptical. It should be noted, however, that many of the gastrogenic diarrheas are not associated with diminution of the pancreatic ferments.

The etiology is gastric according to most authors, though Mayer distinguishes also cases of nervous and of thyroid origin. The gastric disturbance usually consists in achylia, or in motor insufficiency with normal secretion of HCl. The pathogenesis is not clear. Schmidt believes that the faulty gastric digestion leads to secondary changes in the intestine, which in turn bring on the pancreatic disturbance. The lack of the stimulating effect of HCl on the secretion of pancreatic juice cannot be the cause, for it has been shown repeatedly that normal pancreatic function may obtain in the absence of HCl, and moreover many of the reported cases of pancreatic hypochylia have shown normal values for HCl.

The prominent symptoms are diarrhea and loss of weight, and gastric indigestion. The stools show creatorrhea, less often steatorrhea. The ferments in the duodenal contents and in the stools are diminished or absent, and the Schmidt nucleus test is usually positive. There is frequently a marked disturbance of starch digestion, in contrast with the good utilization of starch met with in organic disease of the pancreas. The extreme grade of steatorrhea which is encountered in total exclusion of

pancreatic juice from the intestine is never present, hence the term "hypochylia" is preferable to "achylia."

The condition is distinguished from organic disease of the pancreas by the lack of pain, fever and of diabetes (although alimentary glycosuria may be present), and by the results of opotherapy.

Treatment.—Treatment is very satisfactory, even in long-continued cases. Prompt improvement usually follows the administration of pankreon and HCl, with lavage of the stomach and a bland diet. The ferments return, the Schmidt test becomes negative, and the diarrhea ceases. The fat in the diet need not be restricted, except in the rare cases where there is a marked disturbance of fat absorption. The improvement usually persists after the withdrawal of pancreatic preparations, a point in favor of the functional and temporary nature of the pancreatic disturbance.

Kern and Wiener report favorable results in 1 case from daily injections of pilocarpin in the dose of 0.01 gm., and note that trypsin reappeared in the stool, and disappeared when the injections were discontinued.

CONGENITAL STEATORRHEA

This is a very rare condition, reported only twice, by Garrod and Hurtley, and by Miller and Perkins. It is characterized by the passage of liquid fat with the feces, the so-called "butter-stools," dating from infancy. In Garrod's observation, 2 out of 5 children were affected, the parents being first cousins, and he regards it as a Mendelian recessive character. Miller and Perkins found only 1 child affected.

The stools were bulky and contained both gross and microscopic fat, largely in the form of neutral fat. The fat loss was 25 per cent of the intake. The digestion of protein and starch was normal, and the nutrition and growth of these children was not defective. Trypsin was present in the stools.

On a fat-poor diet the stools became normal. There was no improvement from the use of pankreon or bile salts.

The origin of this condition is obscure. Gross disease of the pancreas is unlikely on account of the normal nutrition and normal utilization of protein. The absorption of fat is involved alone. Garrod ascribes it to an "inborn error of absorption."

ACUTE PANCREATIC NECROSIS (ACUTE PANCREATITIS)

Acute pancreatic necrosis is a remarkable condition, paralleled in no other gland. It is characterized by a rapid necrosis, usually associated

with hemorrhage, and followed in many cases by secondary invasion of bacteria, with suppuration or gangrene. Acute suppurative pancreatitis also occurs independently of necrosis, and will be described later.

The term "acute pancreatic necrosis" is preferable to the older and more usual one of "acute pancreatitis," because it expresses better the nature of the process.

The division into hemorrhagic, suppurative and gangrenous types suggested by Fitz in his classical description, is usually followed in textbooks. It should be understood, however, that they are merely different stages of the same disease.

Pancreatic apoplexy, or rapidly fatal hemorrhage into the pancreas, is a condition often described in the older literature, but is probably always merely acute necrosis in which the hemorrhagic feature is unusually pronounced.

Etiology.—Pancreatic necrosis is nearly twice as common in men as in women, and occurs most often between the ages of twenty and fifty years. The most frequent predisposing cause is cholelithiasis, which was present in 42 per cent of 105 cases collected by Egdahl. This is probably a conservative figure, as small stones in the ducts are easily overlooked. Nordmann found gall-stones in all of his 8 cases.

Next to gall-stones come diseases of the gastro-intestinal tract, especially gastritis, duodenitis and peptic ulcer. These conditions were present in one-third of Egdahl's cases.

Obesity is frequent, and the onset is often a few hours after a hearty meal, at the height of pancreatic secretion. This is in harmony with the observation that acute necrosis is much more easily induced in dogs during the period of digestion. The possible influence of obesity and diet is indicated by the experience of Wilms, who found acute necrosis exceedingly rare in Germany during the latter part of the World War, when fat was hard to obtain and undernutrition was common.

Trauma to the pancreas is an occasional etiologic factor.

Pathogenesis.—Acute necrosis has been produced experimentally by injecting a number of substances into the pancreatic duct, such as gastric or intestinal contents, acids, bile, and bacteria. The common feature of all these experiments seems to be the activation of the trypsinogen within the gland, and this is now agreed to be the cause of the necrosis. Activation is brought about in some of the experiments by injury to the pancreatic cells, the death of which sets free enzymes which change trypsinogen to trypsin. In others it is induced by enterokinase or by bacterial ferments.

Mann and Giordano have shown that the injection of sterile bile will not produce necrosis unless the pressure employed is sufficient to rupture the ducts, and that rupture occurs at a pressure higher than could occur under natural conditions. The injection of infected bile, however, pro-

duces necrosis much more readily than that of sterile bile, as has been shown by Nordmann.

The manner in which gall-stones favor the development of necrosis may now be considered. Opie was the first to describe a case in which a small gall-stone lodged in the orifice of the duodenal papilla had converted the bile duct and the duct of Wirsung into a continuous channel, with entrance of bile into the pancreatic duct. Mann and Giordano, however, conclude from careful anatomical studies that such a mechanism is possible only in a very small percentage of subjects. There are a number of cases, however, in which a small stone has been found lodged low down in the common bile duct, and here it would be possible for bacteria to pass through the wall of the bile duct to the contiguous pancreatic duct, and thus initiate the necrosis through bacterial activation.

In the cases secondary to gastroduodenitis it is possible that the passage of duodenal contents into the pancreatic duct is responsible. Animal experiments have shown that it is impossible in healthy subjects to force intestinal contents into the duct, but it is quite conceivable that in disease there might be a relaxation of the sphincter, due perhaps to the recent passage of a stone or to inflammatory processes.

The fat necrosis is induced by the action of the activated lipase of the pancreatic juice, splitting the fat of the tissue into fatty acids and glycerin.

Pathology.—The appearance of the pancreas varies according to the duration of the disease. In cases examined a few days after the onset, the organ is uniformly swollen and red owing to the presence of extensive hemorrhage. Opaque white round spots and streaks of fat necrosis are usually present in the pancreas, and also in the fat of the transverse mesocolon and the subperitoneal fat, and occasionally at a considerable distance. They are pinhead to pea-sized, or larger and, being easily recognized and pathognomonic of pancreatic disease, are of great diagnostic value to the surgeon. A thin bloody fluid of "beef-broth" appearance is found in the lesser and frequently in the greater peritoneal cavity.

Microscopically there is necrosis, involving part but very rarely all of the gland, and affecting the parenchyma, the interstitial tissue, and the walls of the blood-vessels.

Gangrene of the pancreas may occur, usually at the end of the first or second week. The gland assumes a dark red or black, dry appearance, becoming later soft and moist. The lesser omental cavity is filled with a dark brown fluid in which necrotic pieces of pancreas may be found. Occasionally large sloughs separate from the organ, and may be discharged by way of the intestine. The foramen of Winslow is usually sealed by adhesions, so that general peritonitis does not take place.

If suppuration occurs, the pancreas is the seat of smaller or larger abscess cavities, and the omental cavity may become filled with pus.

Perforation may take place into the stomach, the duodenum or the jejunum. A retroperitoneal abscess in the left loin or, more rarely, a left-sided subphrenic abscess may develop.

Symptomatology.—In a small proportion of cases (about 16 per cent) premonitory symptoms are present in the shape of colicky pain in the epigastrium or left hypochondrium, probably due to mild attacks of acute necrosis. A history of gall-stone colic may be obtained, and necrosis may supervene upon such an attack.

The onset is sudden, with severe pain in the epigastrium, soon followed by vomiting and collapse. The temperature is usually normal or subnormal, though it may be elevated after the first day. The pulse rate becomes increasingly rapid. Constipation and tympanites are frequently marked (25 per cent), so that acute intestinal obstruction is suggested.

The pain is very severe, either continuous or paroxysmal, the usual seat being in the epigastrium or the left upper quadrant, and across the back. The constipation is seldom absolute; flatus is passed and enemata may produce results. The tympanites is most pronounced in the epigastric region, a suggestive feature, but it may become generalized.

Jaundice, usually of slight degree, is sometimes noted. It may be due to pressure of the swollen pancreas on the common duct, or to concomitant biliary disease. Cyanosis is fairly frequent in the later stages, as a result of collapse, and has some diagnostic importance, as it is not common in the diseases for which acute necrosis may be mistaken.

Physical examination may show localized tympanites in the epigastrium, with tenderness here and sometimes in the left loin. A deep-seated transversely situated resistance is often palpable in the region of the pancreas, a sign on which Körte lays great stress. There may be rigidity of the abdominal muscles, but it is less marked than in perforative peritonitis, and is often lacking.

A tumor is seldom palpable before the fourth day; after this time, in cases going on to gangrene or suppuration, a mass may appear in the epigastrium or left hypochondrium, varying in size from that of an orange to a child's head.

A rare sign has been reported by Turner, namely, a bluish discoloration at the umbilicus or in the loin, due to the extravasation of blood, and similar to Cullen's sign in ruptured extra-uterine pregnancy.

Sugar was found in the urine in 18 per cent of Körte's series; it may be present early or late, and is usually transitory. Occasionally a permanent diabetes has been a sequel.

A polynuclear leukocytosis is the rule.

Diagnosis.—The diagnosis is often possible before operation; and should be considered in all cases showing a sudden onset of excruciating pain in the upper abdomen, with vomiting. Important points are localized distention and tenderness in the epigastrium, a deep-seated resistance

corresponding to the site of the pancreas, and in late cases a mass in the epigastrium or left lumbar region. Absence of pancreatic ferments in the duodenal contents, as noted by Crohn, is conclusive, while increase of diastase in the urine is a much less reliable sign. The presence of glycosuria is of great diagnostic importance. Examination of the stools is usually of little assistance, although Pratt and Schmidt have noted a high percentage of neutral fat.

The differential diagnosis is to be made from acute intestinal obstruction, perforative peritonitis, and cholelithiasis. From intestinal obstruction it is distinguished by the early onset of shock, the severity of the pain, the lack of generalized distention, and the fact that flatus is passed and enemata are usually productive. The vomiting is not progressive in pancreatic necrosis, and does not become fecal. Perforative peritonitis gives rise to generalized rigidity and spasm, the tenderness is more marked, and there is often a history of previous gastric or duodenal ulcer, or appendicitis.

The presence of jaundice and the occasional localization of pain in the right hypochondrium may lead to confusion with cholelithiasis, and a differential diagnosis may be impossible in such cases, unless sugar in the urine or pancreatic stools point the way.

Prognosis.—In the severe form of the disease recovery without operation is rare. Death may take place in the first few days, or later after weeks or months as a result of long-continued suppuration and inanition. In the mild form, which is probably not uncommon, temporary recovery occurs, but relapse is frequent, and may assume a severe aspect, or lead to chronic pancreatitis.

Treatment.—For the purpose of treatment the hemorrhagic, suppurative, and gangrenous forms may be considered together. It will be advisable, however, to discuss separately the early stage, in which the symptoms of pain, collapse, and vomiting predominate, and the later stage of abscess formation, when there are chills and hectic fever and a tumor in the epigastrium.

The Early Stage.—In the severe cases operation offers the only hope for the patient, for recovery under medical treatment almost never occurs. It has been recommended by some surgeons to wait until the period of collapse is over before operating, on the ground that the mortality of operation during the stage of abscess formation is much less than that of early operation. But this reasoning is fallacious, because the majority of patients die in the early stage, and only the more favorable cases survive till an abscess appears. The collapse being due to the absorption of toxic products from the diseased pancreas, it is logical to operate at once and remove the source of intoxication.

With regard to the method of operation, there can be no question that drainage of the pancreas, preferably with incision of the gland, is

the best procedure. The statistics of von Mikulicz show this very clearly, for the mortality in the cases without drainage of the pancreas was 80 per cent, while in those with drainage it was only 38 per cent. The incision is made in the middle line, the general peritoneal cavity is walled off with gauze, the pancreas exposed, usually by the gastrocolic route; the swollen gland is incised in several places, the fluid is mopped up with gauze, and drainage is provided, either through the original wound, or through a stab wound in the left loin. Hemorrhage may be controlled by packing with gauze. If jaundice is present, it is important to drain the gall-bladder; gall-stones, if present, should be removed if the condition of the patient permits; otherwise they may be left for a later operation. It is essential that the operation should be rapid and that shock from unnecessary handling of the intestines and exploration of the abdominal cavity should be avoided. The operative mortality in the early stage is high, being 61 per cent in the 59 cases collected by Robson and Cammidge; but it must be remembered that the disease is practically always fatal without operation.

A publication by Körte is of great interest in this connection, embodying, as it does, the experience gained by him and Brentano in a series of 44 personal cases of acute pancreatitis, 38 of which were operated upon. In 4 of the latter the operation was undertaken for disease of the bile-passages, and the lesion of the pancreas was not directly treated; all died. Of the remaining 34 cases 18 got well, giving a mortality of 47 per cent. Contrary to the statements of previous writers, his statistics showed that recoveries were much more frequent in the early stage than later. Thus the mortality in 16 cases operated on in the first two weeks was 31 per cent, in 14 cases in the third and fourth weeks 50 per cent, and in 4 cases in the fifth to seventh weeks 100 per cent. Körte believes that early operations may prevent necrosis and gangrene, especially if pressure is relieved and drainage facilitated by puncturing the gland in several places with a blunt instrument.

The mortality was greatly increased by the presence of necrosis and gangrene, being only 24 per cent in 21 cases without much necrosis, and 85 per cent in 13 cases where extensive destruction of the gland had taken place.

In a certain number of cases the disease runs a milder course (the subacute form of Robson and Cammidge), the onset being less severe and collapse absent. Here it is allowable to wait until an abscess has formed; indeed, the patients usually do not come to the hands of the surgeon until suppuration has occurred. Occasionally the inflammation subsides without abscess formation, and in such cases the question of purely medical treatment may be considered. Since, however, relapses are common and may prove fatal, it is probably better to operate even in the absence of abscess formation.

The Late Stage.—Treatment here consists simply of opening the abscess and providing drainage. The incision is made over the most prominent part of the abscess, which will usually be in the middle line, but not infrequently in the left loin. The operative results in this stage are decidedly better than in the early stage, Villar's statistics showing a mortality of 38 per cent in 53 operations. The chances for recovery are best where there is a single abscess, while cases with multiple abscesses or diffuse suppuration almost always die.

Dietetic and Symptomatic Treatment.—Most cases will require morphia for the pain. Cathartics are not indicated, but the lower bowel should be emptied by enemata. Lavage of the stomach may be employed against the vomiting. The collapse is to be combated by the usual measures. During the early stage it is better not to attempt feeding by mouth, but to resort to rectal feeding. There are two reasons for this: (1) because the vomiting is often uncontrollable; (2) because it is desirable to place the pancreas at rest, and this is best done by avoiding the chief stimulant to pancreatic secretion, the presence of food in the duodenum. Later on skimmed milk or buttermilk would be an appropriate form of nourishment. After recovery from the immediate effects of the acute disease, chronic lesions of the pancreas sometimes remain, especially diabetes or insufficiency of the pancreatic secretion; directions for the treatment of these conditions will be found in the chapter on Diabetes and in the section on the Diet in Chronic Pancreatitis.

SUPPURATIVE PANCREATITIS

Abscess formation of the pancreas often occurs in pancreatic necrosis, owing to the invasion of bacteria. It is also met with as a primary process, usually as a result of ascending infection of the ducts, much more rarely in the form of metastasis by way of the blood-stream. Obstruction of the ducts favors the entrance of bacteria; and many cases are met with as a result of such obstruction by gall-stones, pancreatic calculi, or malignant disease. The suppuration frequently extends to the omental cavity, which becomes distended with pus.

The symptoms may be those of acute pancreatic necrosis. In some cases the onset is violent with chills and high fever, while in others it is insidious, and pain and fever may be moderate or even lacking. A palpable tumor is present in only one-fourth of the cases, while in others deep-seated resistance and tenderness point to the pancreas as the seat of the trouble.

Glycosuria and signs of deficient external secretion may be present, but more often they are missed, owing to the considerable amount of normal pancreatic tissue remaining.

The abscess may rupture into the stomach or intestines, or into the general peritoneal cavity. Thrombosis of the portal vein may occur.

The *treatment* is surgical. Incision and drainage of the abscess may lead to recovery, but where diffuse suppuration or multiple abscesses are present, a fatal outcome may be expected.

ACUTE NON-SUPPURATIVE PANCREATITIS

This condition has nothing to do with acute pancreatic necrosis, though often confused with it. It occurs in association with acute infectious diseases, most frequently with mumps.

1. **In Epidemic Parotitis.**—The close physiological and anatomical resemblance of the two glands explains the occurrence of metastasis to the pancreas.

The pathology is probably similar to that of the affected salivary glands, that is, edematous swelling with infiltration of lymphocytes around the ducts. In the only reported case with autopsy, that of Lemoine and Lapasset, the pancreas was greatly enlarged, edematous and congested, weighing 190 gm.

The frequency of the complication varies in different epidemics, and with the criteria demanded for the diagnosis. If one looks for it, it is certainly far from rare. Simonin reported it in 1.3 per cent among soldiers with mumps, while Moutier found it much more frequently, noting its occurrence in 70 of 600 cases among soldiers, or 12 per cent. He diagnosticated pancreatitis in all cases showing pain near the umbilicus with tenderness on palpation over the pancreas. The more severe cases showed also high fever, nausea and vomiting, diarrhea or constipation, prostration and occasionally jaundice; in one there was transitory glycosuria. An abdominal mass was rarely palpable. The onset was usually on the fourth to the seventh day of parotitis, and was marked by an increase of the fever. He made no functional studies, but cases are on record by Gross and Mayer, in which absence of ferments and fatty stools or creatorrhea were present. In a case reported by Farnam, the abdominal symptoms were so severe that laparotomy was performed. The pancreas was found much enlarged and inflamed, and general peritonitis was present, with Streptococcus viridans in the exudate. Recovery followed. This is the only operative case on record. (A good bibliography accompanies this article.)

The duration of symptoms is usually only a few days, when recovery takes place. The only fatal case in the literature is that of Lemoine and Lapasset. No after effects have been noted.

The treatment is purely symptomatic, consisting of hot applications and morphia for the pain.

2. **Acute Pancreatitis in Other Infectious Diseases.**—Acute pancreatitis has been described also in connection with typhoid fever, influenza and pneumonia, but very rarely. Mayer reported 1 case after influenza, another on the eighth day of pneumonia, and 4 complicating spirochetal icterus. All of these cases showed fatty stools and diminution or absence of ferments. One of the cases complicating spirochetal icterus was fatal, and showed multiple hemorrhages and extensive destruction of the parenchyma of the pancreas.

The pain was very severe in all of Mayer's cases, either continuous or paroxysmal, located in the epigastrium, radiating to the sacrum, and not associated with tenderness. Abdominal rigidity was absent and vomiting was rarely noted.

The differential diagnosis from pancreatic necrosis depends on the close connection with an acute infectious disease, and the presence of fever at the onset, at a time when the temperature is normal or subnormal in necrosis.

The treatment is dietetic and symptomatic. Pancreatic preparations are indicated. Operation is unnecessary in most cases, since recovery under medical treatment seems to be the rule.

CHRONIC PANCREATITIS

Chronic pancreatitis occurs in the form of a chronic inflammatory process involving chiefly the interstitial tissue. Opie distinguishes two types, the *interlobular,* in which the process involves the bands of connective tissue which run between the lobules of the gland, and the *interacinar,* in which the connective tissue proliferation takes place between the acini. In the interlobular type the islands of Langerhans are not involved until late in the disease, if at all, while in the interacinar form involvement of the islands is apt to occur early, with diabetes as the consequence. The main causes of chronic pancreatitis are infections from the intestine or from the biliary tract by way of the duct of Wirsung; obstruction of the ducts, as by tumors of the head of the pancreas, gallstones in the duodenal papilla, or pancreatic calculi; alcoholism, syphilis, and arteriosclerosis. It may be a sequel of acute pancreatic necrosis. Localized pancreatitis may occur by extension from a gastric or duodenal ulcer. The Laennec type of cirrhosis is very frequently accompanied by chronic pancreatitis, both being probably due to a common cause, alcohol. Hemochromatosis is usually associated sooner or later with chronic pancreatitis and diabetes.

The symptoms of chronic pancreatitis vary considerably according to the part of the gland affected. Perhaps the majority of cases show no definite symptoms of pancreatic disease during life, and are first discov-

ered by the pathologist. Clinically the condition is met with most frequently as a complication of infections of the bile passages, and here the symptoms of pancreatitis will be masked by those of the biliary infection, and the head of the pancreas will be found enlarged and hard at the operation undertaken for gall-stones. In another type which is rather rare, there is chronic jaundice due to pressure of the inflamed head of the pancreas on the common bile duct, and here there are attacks of pain in the epigastrium, and sometimes the enlarged gland may be felt as a hard, tender tumor. In such cases the diagnosis from cancer of the pancreas is often difficult, even after the abdomen has been opened. Or, again, the pressure may be exerted on the ducts of Wirsung and Santorini, and exclusion of the pancreatic juice from the intestine take place, resulting in characteristic disturbances of digestion, with the passage of very bulky stools, showing on microscopic examination large numbers of droplets of neutral fat (steatorrhea) and many undigested muscle fibers (creatorrhea). In such cases, if a considerable amount of fat is given in the diet (about 100 gm.), there will usually appear in the stools masses of fat visible to the naked eye, a phenomenon which is practically pathognomonic of absence of the pancreatic juice from the intestine.

Hypo-acidity or anacidity of the stomach is very common, occurring in about 50 per cent.

In many cases, however, there is neither jaundice nor complete obstruction of the pancreatic ducts, and then the clinical diagnosis becomes very difficult. It is possible in those cases with glycosuria and attacks of pain situated in the epigastrium, and may be made with some reserve if there are pain, emaciation, and *alimentary* glycosuria. Guleke emphasizes the character of the pain, which in typical cases is agonizing, so that the victim does not dare to move or eat, and lies with the legs drawn up. It is often accompanied by vomiting. Pancreatitis may be suspected in those cases of alcoholic cirrhosis showing marked glycosuria after the administration of glucose, even in the absence of abdominal pain.

Treatment of Chronic Pancreatitis.—The first indication in this, as in all disease, is to find the cause, and remove it if possible. Catarrh of the stomach and duodenum should receive careful attention, and the underlying causes should be eliminated. In all cases of cholelithiasis in which there is reason to suspect involvement of the pancreas, the gall-stones should be removed and the gall-bladder drained. This in itself is usually sufficient to bring about a cure of the pancreatitis. Thus, in a case of cholelithiasis seen by the writer, with slight jaundice and small amounts of sugar in the urine, the glycosuria disappeared after the removal of a gall-stone from the cystic duct. Syphilis, although a rare cause of pancreatic disease, should be borne in mind, for specific treatment may prove curative.

Medical Treatment.—In those cases which have not reached the later stage, in which cure by any means is impossible, an attempt should be made to bring the inflammatory process to a standstill by means of rest in bed, heat applied to the epigastrium (either in the shape of poultices or the thermophor), and appropriate diet. Medical treatment should not be persisted in longer than six weeks after the appearance of jaundice, on account of the possibility of the development of a tendency to hemorrhage.

The *diet* in chronic pancreatitis should be adapted to the circumstances of the individual case, depending on the presence or absence of obstruction of the common bile duct and the pancreatic ducts, and of glycosuria. If all the ducts are open the diet should be simple and easily digested; that is about as much as can be said at present. It remains for future investigations to show which form of diet puts least work upon the pancreas. It is known to be sure that, as a rule, in human beings a diet of fat and protein calls forth the smallest amount of pancreatic juice, and a diet of carbohydrates the largest; but, as the concentration of the pancreatic juice varies considerably under different conditions, it probably would be a mistake to prescribe an antidiabetic diet.

If the bile duct is obstructed, but the pancreatic ducts are open, as shown by the presence of jaundice with an excess of fatty acid crystals, but no gross fat and few neutral fat droplets in the stools, the diet should be that of simple jaundice, that is, with fats restricted.

When the stools are bulky and show fat visible to the naked eye, and under the microscope large numbers of neutral fat droplets and undigested muscle fibers, in other words, when the pancreatic juice is absent from the intestine, the diet should consist largely of milk, eggs, bread, cereals, and carbohydrates, for in such cases casein, egg-albumin, and vegetable protein are better digested than is meat, and emulsified fats are probably better digested than are the non-emulsified. Carbohydrates are well digested in the absence of pancreatic juice, and may be given freely unless glycosuria is present.

Opotherapy.—As was stated at the beginning of this chapter, the administration of raw pancreas or of active pancreatic extracts often increases very materially the absorption of fat and of protein in cases where the pancreatic juice is deficient. Quite large doses should be given, from 1 to 3 gm. (15 to 45 gr.) three times a day after meals, using pankreon, or pancreatic extract with calcium carbonate in equal parts. If achlorhydria is present, it is unnecessary to give calcium carbonate. If the extract is without effect raw pancreas should be tried, using the whole gland of a pig or sheep, procured fresh each day. Where jaundice is present the use of desiccated bile or of bile salts is indicated, as the fat-splitting action of the pancreatic juice is greatly enhanced by the presence of bile.

Surgical Treatment of Chronic Pancreatitis.—Surgical treatment is indicated: (1) in all cases which are due to gall-stone disease; (2) in the absence of gall-stones in those cases where jaundice exists and medical treatment is without avail; and (3) where there are repeated attacks of violent pain in the epigastrium.

In the cases associated with cholelithiasis removal of the gall-stones with drainage of the biliary passages for a few weeks usually results in a cure. In advanced cases cholecystenterostomy, as advocated by Robson, or cholecystgastrostomy (Kehr), is preferable, as it affords permanent drainage of the bile passages. These latter operations are also indicated in cases of pancreatitis with jaundice due to compression of the common bile duct by the head of the pancreas. The anastomosis should be made, if possible, between the gall-bladder and the duodenum, or the upper part of the jejunum. Anastomosis with the transverse colon is undesirable for two reasons: (1) because the bile is not available in the small intestine for digestive purposes; (2) on account of the danger of infection of the bile passages from the colon. W. J. Mayo states that cases due to chronic cholecystitis without stones are only temporarily relieved by biliary drainage, but are cured by removal of the gall-bladder. This may be explained by the relaxation of the sphincter of the papilla, with continuous passage of bile into the intestine, which Judd and Mann have shown to take place after cholecystectomy in animals. If biliary obstruction exists, Mayo advises drainage of the gall-bladder, rather than its removal.

Archibald insists on the value of prolonged biliary drainage (four weeks or more) in all cases of chronic pancreatitis, whether associated with biliary disease or not.

In cases due to peptic ulcer, gastro-enterostomy is indicated, and may lead to a cure of the pancreatitis.

Where jaundice is intense and of long duration the danger of hemorrhage at the operation, or afterward, may be best averted by daily intravenous injections of 5 c.c. of a 10 per cent calcium chlorid solution over a period of three days, as practised by Walters. By this means the prolonged clotting time of the blood can be almost always brought down to the normal level. It may be necessary to give one or two injections after the operation, being guided by the clotting time, as the effect is temporary. Cases not yielding to this treatment should be transfused with blood shortly before operation. Hemorrhage from the wound after operation may be controlled by packing combined with the local use of adrenalin.

In a few instances operation has been undertaken in the absence of jaundice for the relief of attacks of severe epigastric pain; in the case of Martina partial decapsulation of the pancreas, which was encased in a mass of dense fibrous tissue, restored the patient to health.

The presence of a moderate amount of glycosuria is not a contra-

indication to operation, but rather the contrary, for in cases not too far advanced a cure of the pancreatitis may be expected, and with it a disappearance of the sugar from the urine. In other cases the patient is apparently restored to health, but the pancreas has been too much damaged for restitution to the normal, and the diabetic condition persists. It goes without saying that cases of grave diabetes should not be operated upon, except as a last resort.

The results of surgery in the hands of skilled operators have been most encouraging. Thus Robson states that his operative mortality in 1904 was 3.9 per cent. Of 55 patients operated on for chronic pancreatitis with gall-stones, 3 died soon after operation; all were in very poor condition at the time of operation; of the 52 who recovered, 48 were living and well when last heard from, 1 nine and one-half years after operation had diabetes, 1 died of cirrhosis of the liver, and 2 others of diseases not related to the pancreas. Out of 46 cases of pancreatitis without gall-stones, 1 died after operation, 6 did not reply to letters, the others were all well, with the exception of 1 patient, who developed glycosuria, and 1 who showed "signs of permanent damage to the pancreas by the urinary (that is, Cammidge) test, and one who has anemia suggestive of the pernicious type." Since then Robson's mortality has sunk to 2 per cent, a truly brilliant record. Kehr's results are not so striking, perhaps because his material is different. Of 5 cases of pancreatitis without gall-stones, all were cured, while in 54 cases associated with gall-stones the mortality was 17 per cent. He prefers anastomosis of the gall-bladder with the stomach to that with the duodenum for technical reasons; apparently the entrance of the bile into the stomach has not proved injurious to the digestion in his patients. Where the stone is in the common duct he prefers to excise the gall-bladder and drain the hepatic duct, while Robson retains the gall-bladder if possible, on the chance that cholecystenterostomy may be required later.

PANCREATIC INFANTILISM

Byrom Bramwell has described a case of stunted growth with diarrhea and fatty stools, in which the administration of pancreatic extract over a long period was accompanied by a very rapid increase in weight and height, and the development of the sexual organs, which were previously in an infantile state. He therefore ascribed the infantile condition to defective pancreatic secretion. Since then similar cases have been reported by Thomson, Rentoul and L. Brown; in Brown's case congenital syphilis was present, and chronic pancreatitis was found at autopsy.

TUBERCULOSIS OF THE PANCREAS

Tuberculosis of the pancreas is a rare condition. It is always secondary to tuberculous disease elsewhere in the body. It occurs in two forms: as miliary tubercles and as large caseating masses. The latter probably originate in the lymphoid tissue of the gland. Very rarely the tuberculous mass may be large enough to palpate, as in the case of Sendler, who successfully removed a tuberculous lymph-node the size of a walnut from the head of the pancreas.

SYPHILIS OF THE PANCREAS

Syphilis of the pancreas is frequently found at autopsy in cases of congenital syphilis, either in the form of diffuse infiltration or of gummata, but does not give rise to special symptoms. In the adult gross pancreatic syphilis is rare, and occurs either in the form of gummata, or of diffuse induration similar to syphilitic cirrhosis of the liver, with which it is often associated.

The clinical picture has been drawn by Walter-Sallis, Wile and others. The symptoms are similar to those of chronic pancreatitis, but with the following differences: A tumor is much oftener palpable, being noted in one-half the cases, and glycosuria, which is rare in pancreatitis (except in the form due to pancreatic calculi), is also present in 50 per cent. Jaundice is the rule, and fever is not uncommon.

The diagnosis is made on the above points and on evidence of syphilis, and is confirmed by the success of specific treatment.

It is important to bear the possibility of pancreatic syphilis in mind, for complete cure may follow antisyphilitic treatment, even when diabetes is present, as in a case reported by Singer. Moffitt's 2 cases of diabetes in syphilitics, cured by specific treatment, probably belong in this category.

Though clinical syphilis of the pancreas is apparently rare, a recent study by Warthin shows that this organ is frequently involved in the syphilitic process. He found histological changes in the pancreas in all of 150 cases of syphilis. The lesions noted were small foci of round-cell infiltration with plasma cells, scattered patches of fibrosis, with destruction of the islands in places, and atrophy of the acini. The blood-vessels showed varying degrees of sclerosis. Spirochetes were demonstrated in the pancreas in one case.

In 6 cases of diabetes definite syphilitic pancreatitis was demonstrated. Warthin believes that syphilis is the most common cause of chronic pancreatitis. Opie's experience was quite different, for he found no case in

the autopsy records of the Johns Hopkins Hospital in which chronic pancreatitis was associated with visceral syphilis.

PANCREATIC CALCULI

Stones of the pancreas are very rare. They are situated in the ducts, and are frequently multiple. They are easily distinguished from biliary calculi, being grayish white, rough and friable, and composed chiefly of calcium carbonate. They are due to chronic infection and obstruction of the ducts, and lead to chronic pancreatitis. Diabetes is associated more frequently than in any other disease of the pancreas, with the exception of syphilis, being noted by Lazarus in 45 per cent.

There may be no symptoms during life, or diabetes may be present alone. In some cases, however, periodic attacks of severe epigastric pain occur, which may be associated with typical pancreatic stools. Jaundice is rarely present.

A tentative diagnosis may be made if there are periodic attacks of pain associated with diabetes and the signs of deficiency of the pancreatic juice, provided syphilis is excluded. The diagnosis is rendered certain by the passage of pancreatic calculi in the stools, or by the presence of shadows in the region of the pancreas in the X-ray picture, as noted by Assmann and Pförringer.

Medical treatment can be only palliative. Pilocarpin, which increases the flow of the pancreatic secretion, may be tried, but is not without danger. A number of successful operations for the removal of calculi have been recorded by Gould, Allen, Moynihan, Robson and others. For the operative methods the reader is referred to Robson and Cammidge, page 485. Link found the ducts filled with minute stones, too numerous for removal, and performed the novel operation of pancreostomy, with the formation of a permanent fistula. The patient obtained relief from the pain, and gained 20 pounds in weight.

PANCREATIC CYSTS

True cysts of the pancreas have an epithelial lining, and are either retention cysts, due to obstruction to the outflow of pancreatic secretion, or cystic tumors, proliferating cystadenomata. The true cysts are of rare occurrence, compared with the frequency of pseudocysts, which have no epithelial lining and are probably due to the corrosive action of the pancreatic juice.

Pseudocysts constitute the great majority of pancreatic cysts, and are due in about one-third of the cases to trauma, and in the other two-

thirds to inflammatory conditions in the pancreas. They are situated usually either between the anterior surface of the gland and the peritoneum, or in the omental bursa. One or more of the ferments of the pancreas is usually, but not always, present in the contents.

Echinococcus cysts of the pancreas have been reported, and have been cured by incision and drainage.

The cyst usually occupies the omental bursa, and grows forward, presenting between the stomach and the colon. More rarely it appears above the stomach, and least frequently in the lower abdomen below the colon.

Symptoms.—Pain is one of the most common symptoms, but may be lacking. It is usually situated in the epigastrium. Pressure symptoms are not uncommon; thus the stomach may be involved, with dyspepsia and vomiting, the colon with constipation or even intestinal obstruction, the portal vein with ascites, or the inferior vena cava with edema of the legs. Jaundice is unusual.

Functional disturbances of the pancreas are noted in only a small percentage of cases. There may be steatorrhea or creatorrhea, or rarely diabetes. Emaciation is fairly common.

The tumor is palpable in most instances, and presents in the epigastrium or the left hypochondrium, or rarely below the umbilicus. It is rounded and usually fluctuating, and varies in size up to that of a man's head.

It is usually neither freely movable from side to side, nor with respiration, but there are exceptions to this rule. A sudden disappearance of the tumor, coinciding with the discharge of a watery fluid by the bowel, has been noted occasionally. Marked changes in the size of the tumor from time to time, without diarrhea, have been recorded, and are regarded as characteristic of pancreatic cysts.

Diagnosis.—Cyst of the pancreas is a rare disease, and a good many of the cases so diagnosticated turn out to be something else. It is to be distinguished from cysts of the liver, spleen, and mesentery, hydronephrosis of the left kidney, and solid tumors of the neighborhood. It has been confused with a dilated gall-bladder, but there is little excuse for this mistake. Very large cysts might be confused with cysts of the ovary. A correct diagnosis usually may be reached by attention to the following points:

1. A history of direct injury to the epigastrium, or of a previous attack resembling acute pancreatic necrosis, is very suggestive of a pseudocyst of the pancreas.
2. Inflation of the stomach and colon is helpful, the position of the tumor behind the stomach and above the colon being indicative of a pancreatic origin.

3. The Roentgen ray offers valuable evidence, as shown by Albu. In the case of large cysts the stomach after a barium meal shows as a narrow rim of semicircular form on the left side of the cyst.

4. Signs of defective pancreatic function, including diabetes, are conclusive, but unfortunately they are rarely present.

The presence of ferments in the contents of the cyst is of less diagnostic value than was formerly thought, for they may be absent in pancreatic cysts and present in cysts of other origin.

Treatment.—The tapping of pancreatic cysts has fallen into deserved disuse on account of its failure to cure and its dangers. The two methods in vogue now are: (1) extirpation, and (2) incision and drainage.

Extirpation.—Complete extirpation is seldom possible, owing to the frequency of adhesions. It is necessary for cure only in the cases of true cysts, where the epithelial lining continues to secrete after incision and thus prevents the obliteration of the cyst by granulation tissue. According to Goebel, extirpation should not be attempted except under favorable circumstances, as where the cyst has a pedicle or is situated in the tail of a movable pancreas, for the mortality is high, 10.7 per cent for complete extirpation, 55.5 per cent for partial extirpation, that is, where the operation had to be left uncompleted on account of technical difficulties.

Incision and Drainage.—This operation is usually done in one stage. The incision is made over the most prominent part of the cyst, usually in front, rarely in the loin. The cyst is exposed by incision of its peritoneal coverings, and the contents evacuated through a large trocar, after protection of the abdominal cavity by packing. The opening is then enlarged and the edges of the cyst are sutured to the parietal peritoneum. The insertion of a large drainage tube concludes the operation. The skin may be protected from the corrosive action of the pancreatic secretion by the application of stearate of zinc, or antiseptic ointments.

The results after incision and drainage are good, as a rule. Goebel states that a cure resulted in 96.4 per cent of 190 cases collected from the literature, but this figure is probably far too high, as the later history of many of the cases is unknown. Robson and Cammidge give the operative mortality as 11.6 per cent. The cyst cavity gradually closes up by the collapse of the walls and the formation of granulation tissue, and after about a month only a small fistula remains, which usually closes entirely later. Recurrence of the cyst is rare, except in the case of true cysts. The injection of irritating fluids into fistulæ to promote closure may be dangerous, as in a case of Lazarus, in which death resulted from the injection of a silver nitrate solution. Persistent fistulæ are often to be healed by the use of antidiabetic diet (see section on Pancreatic Fistula), or by extirpation.

TUMORS OF THE PANCREAS

The most common new growth of the pancreas is carcinoma. Other tumors, such as sarcoma, fibroma and adenoma, are great rarities.

Carcinoma of the Pancreas.—Carcinoma occurs in three forms: (1) primary; (2) by extension from neighboring organs, usually the duodenum or stomach; and (3) metastatic. The first two are fairly common, but metastases are unusual and of no clinical importance.

Extension from the neighborhood does not usually lead to pancreatic symptoms, except in the case of cancer low in the duodenum or at the papilla of Vater, in which case it may be impossible even at autopsy to ascertain the point of origin.

Cancer of the pancreas is an uncommon but not a rare disease, occurring in about 1/10 per cent of all autopsies. About 1 out of each 100 cases of cancer is located in the pancreas. It occurs twice as often in men as in women.

Pathology.—The growth arises from the ducts, or from the acini, or rarely from the islands of Langerhans. It usually takes a scirrhous, less frequently a medullary, rarely a colloid, form. It is situated in the head of the gland in about three-quarters of the cases; it may infiltrate the whole gland, or be confined to the body or tail.

Pressure on the ducts leads to chronic interlobular pancreatitis of the part distal to the growth, with diabetes if the islands are destroyed. Pressure on the common bile duct is frequent in cancer of the head of the pancreas, and leads to jaundice and dilatation of the gall-bladder. Pressure on the portal vein may occur, with the production of ascites, and the duodenum may be involved, with consecutive dilatation of the stomach.

Metastases are found at autopsy in about three-quarters of the cases. They are usually stated to occur by way of the lymphatics, and to affect chiefly the liver and regional lymph-nodes; but a recent study by Adams indicates that metastasis by way of the blood-vessels is common. He found extensive metastases in 6 out of 8 cases, in 2 of which many organs were involved.

Symptoms.—The usual symptoms of cancer are present, and cachexia, with rare exceptions, is marked and rapid. Anorexia, nausea and vomiting are often noted. The tumor is not usually palpable owing to its small size and deep location. Pain is the commonest and earliest symptom, but may be lacking. It is situated in the epigastrium, occasionally in the right or left hypochondrium, and may radiate to the back, shoulders or sacrum. It may be mild or extremely severe. Fever, usually of moderate degree, is present in a considerable proportion of cases. Occult blood is frequently to be found in the stools.

The special symptomatology of cancer of the pancreas occurs only

when the head of the gland is involved, and pressure is exerted on the common bile duct or the pancreatic ducts, or both. In such cases jaundice is the most conspicuous feature, occurring in about 75 per cent of cases of cancer of the head of the pancreas. It is progressive and leads finally to a greenish color of the skin, with complete absence of bile pigment in the stools. The gall-bladder becomes dilated, and is usually palpable during life.

Frequently the pancreatic ducts are obstructed, and the characteristic bulky pancreatic stools are observed, with steatorrhea and creatorrhea, and absence of ferments. These signs were present in all of 5 cases studied by the writer, and their rarity in the literature is due to faulty observation.

Stenosis of the duodenum occasionally occurs, and leads to dilatation of the stomach and vomiting. Ascites is met with in about 10 per cent.

Glycosuria is present in about 25 per cent, and when present is a great aid in diagnosis. It usually occurs late in the disease, and yields rather readily to dietetic treatment.

Diagnosis.—The diagnosis depends on the finding of signs of pancreatic disease, with features pointing to malignancy. In general it may be said that the conjunction of jaundice with a palpable gall-bladder and signs of deficiency of the pancreatic juice, especially in the presence of glycosuria, renders the diagnosis of cancer of the pancreas almost certain. It is true that chronic pancreatitis may give a similar picture, but so rarely that the chance of error is slight. Ascites is in favor of malignancy, provided that cirrhosis of the liver can be excluded.

The presence of a palpable tumor renders the diagnosis almost certain, although chronic pancreatitis and syphilis are still remote possibilities. The finding of metastases in the liver or elsewhere is, of course, conclusive.

The jaundice of pancreatic disease is distinguished from that due to obstruction of the common duct from other causes by the character of the stools, and often by the presence of achlorhydria, for simple obstruction of the bile duct usually leads to hyperchlorhydria. The presence of a dilated gall-bladder, according to Courvoisier's law, is valuable evidence of malignancy as against stone in the common duct.

The Roentgen ray may be of assistance, not by showing the tumor itself, but an accompanying dilatation of the duodenum, which remains filled with barium for a considerable time. This finding merely indicates gross disease of the pancreas, being met with also at times in chronic pancreatitis and in acute necrosis. Extension of the dilatation to the stomach, however, is almost certain evidence of malignancy.

Carcinoma of the body and tail of the pancreas cannot be diagnosticated during life, unless a tumor is palpable.

Surgical Treatment of Tumors of the Pancreas.—Cancers are very seldom suitable for extirpation, on account of the technical difficulties of removing the head of the pancreas, which are often enhanced by the

presence of adhesions and the involvement of lymph-nodes and other adjacent structures. Thus Kehr, in an experience of 71 cases, did not meet with a single one in which removal was possible. In a few instances carcinomata have been successfully removed, but death has taken place within a few months from recurrence of the growth.

Exploratory laparotomy is usually justifiable because of the impossibility of distinguishing with absolute certainty by other means between chronic pancreatitis and cancer. If on exploration there are metastases or the diagnosis seems certain, it is probably best to close the abdomen without attempting more. The operation of cholecystenterostomy or cholecystgastrostomy has been often performed, for the sake of relieving the jaundice. On account of the very high mortality it has been given up by most surgeons; Kehr, however, advocates it, having operated on 10 such patients, who lived two years in comparative comfort after the formation of an anastomosis between the gall-bladder and the stomach. He does not state, however, how many others died as the immediate result of the operation.

Benign tumors situated in the body or tail of the pancreas have been removed successfully in a few instances, such as the case reported by Finney, who has collected the literature on the subject. These cases are important as showing that operations on the pancreas can be performed without much danger, providing that the peritoneum is protected by packing from the action of the pancreatic juice, and adequate drainage is established. Thus Finney was able to resect most of the pancreas along with the tumor, and suture the head and the tail of the gland together.

Medical Treatment of Carcinoma of the Pancreas.—The diet should be the same as that outlined under Chronic Pancreatitis. Pancreatic preparations are indicated if there is deficiency of the pancreatic juice, and fel bovis or bile salts if jaundice is present. Morphia may be required for the pain, and warm bran baths with the addition of bicarbonate of soda (6 ounces to 30 gallons of water) for the itching.

INJURIES TO THE PANCREAS

Injuries to the pancreas may be considered under three headings, namely, (1) lacerated wounds due to contusions of the abdomen, the so-called subcutaneous rupture of the pancreas; (2) bullet wounds; and (3) penetrating wounds.

Rupture of the Pancreas.—The pancreas is deeply situated and admirably protected from external violence. It is sometimes ruptured, however, as a result of direct force applied to the epigastrium or adjacent parts; such cases have been reported after the following accidents: being caught between two cars, being run over, kicked by a horse, or struck in

the epigastrium by a blunt object. Most often other abdominal organs are injured as well, especially the liver, spleen, or kidneys. In a few cases isolated rupture of the pancreas occurs, and is the cause of the fatal outcome, either by hemorrhage or from the effects of the extravasated pancreatic secretion. More often trauma is the cause of a slight bruising of the pancreas, with leakage of blood and pancreatic juice into the omental bursa, and the subsequent formation of a pseudocyst.

The diagnosis of pancreatic rupture is extremely difficult. Usually the symptoms point merely to some grave intra-abdominal injury. Epigastric muscular spasm and tenderness is a very early symptom, followed within a few hours by pain, vomiting, increasing pallor, and collapse. The temperature is normal at first, but may be elevated later. The presence of a tumor in the epigastrium may lead to the right diagnosis, as in the case of Blecher. Sugar has been observed in the urine in 3 cases only, after the operation. After the abdomen is opened the oozing of blood from the omental bursa, the presence of a tumor in the region of the pancreas or of fat necrosis should lead to the correct diagnosis, which is very important, as the life of the patient depends upon it.

Treatment.—Rupture of the pancreas, if extensive, is probably always fatal unless treated surgically. Garre, in 1905, published the first case cured by operation; Heineke, two years later, was able to collect 19 cases of isolated rupture of the pancreas, and since then a number of cases have been reported. Five cases were not operated upon; all died. Of the 19 cases undergoing operation, 13 recovered. Six died, but in 3 of these the rupture of the pancreas was not discovered at the operation, 2 came late to operation in a desperate condition, and 1 recovered from the pancreatic condition, to die of pneumonia five months later. *Thus every case with early operation and proper treatment of the pancreas recovered.*

Method of Operation.—After the removal of the extravasated blood and the control of hemorrhage, by packing if necessary, the condition of the gland is examined. If the edges of the tear are clean-cut, suture is indicated; otherwise packing. In suturing the duct should be avoided. Drainage must be provided in any case, as even after the most careful suture there is always leakage of pancreatic secretion, the escape of which must be provided for. A pancreatic fistula always forms after the operation.

Bullet Wounds of the Pancreas.—The pancreas is sometimes involved in bullet wounds of the abdomen, almost never alone. Such wounds are to be treated in the same way as rupture of the pancreas. The results have been encouraging, 9 patients recovering out of a total of 15 operated upon, according to Robson and Cammidge, and, in 3 of those dying, the wound of the pancreas was not discovered at the operation.

Penetrating Wounds of the Pancreas.—The pancreas is occasionally wounded by thrusts with a knife or bayonet. Almost invariably a portion

of the pancreas has protruded from the abdominal wound, and the general peritoneal cavity has not been exposed to the action of the pancreatic juice. This is probably the reason that almost all the reported cases recovered. In some the exposed portion of the pancreas has been resected, in others it has been cleansed and returned to the abdominal cavity. Drainage is necessary in all cases.

PANCREATIC FISTULA

Fistula is a not infrequent sequel of operations on the pancreas, of all sorts, particularly after those for cyst or injury. The secretion from the sinus usually contains the pancreatic ferments, and is extremely irritating to the skin. Sometimes the fistula becomes temporarily obstructed, and then there is abdominal colic from the retention of the pancreatic fluid.

Treatment.—Until recently fistula of the pancreas was treated only on general surgical principles, often without success. The injection of irritating substances, such as tincture of iodin and silver nitrate, may promote closure, but has not proved without danger. Sometimes a secondary operation has been performed and the fistulous tract dissected out, or the fistula has been transplanted into the stomach, or into the gall-bladder, and the gall-bladder connected with the stomach.

Such measures, however, have become unnecessary for most cases since the valuable discovery by Wohlgemuth that the pancreatic secretion in man can be influenced to a large extent by diet and by drugs. This observer, experimenting on a case of pancreatic fistula, got very similar results to those obtained by Pawlow in dogs: the secretion was greatest on a diet of carbohydrates, less on a protein diet, and ceased altogether when fats alone were given. Hydrochloric acid increased and sodium bicarbonate diminished the secretion. The use of a strict antidiabetic diet, with sodium bicarbonate in dram doses both before and after each meal, resulted in the prompt and permanent closure of a fistula of long duration. Since then this treatment has been employed with striking success in a number of cases; fistulæ that had persisted for years were closed in a few days or weeks. In a few instances, however, the treatment has failed. The diet should be kept up for a while after the fistula has closed, or else it may break out again. If no result is obtained in six weeks it is useless to continue the treatment longer.

Culler has reported the prompt closure of fistulæ in 2 cases following daily X-ray treatments. His cases were both of short duration.

REFERENCES

Adams, F. D. Arch. Int. Med., xxvii, 175, 1921.
Albu, A. Berl. klin. Wchnschr., lv, 307, 1918.
Allen, L. W. Ann. Surg., xxxvii, 740, 1903.
Archibald, E. Journ. Am. Med. Ass., lxxi, 798, 1918.
Assmann, H. Fortschr. a. d. Geb. d. Röntgenstrahlen, xviii, 242, 1911.
Bickel, A. Verhandl. d. Kong. f. inn. Med., xxiv, 490, 1907.
——— Therap. Rundschau, ii, 629, 1908.
Blecher. Verhandl. d. deutsch. Gesellsch. f. Chir., xxxv, 117, 1906.
Bramwell, B. Scot. Med. & Surg. Journ., xiv, 321, 1904.
Brown, L. W. Practitioner, xxii, 233, 1905.
Brown, T. R. Johns Hopkins Hosp. Bull., xxv, 200, 1914.
Brugsch, T. Ztschr. f. klin. Med., lviii, 518, 1906.
——— Ztschr. f. exper. Path. u. Therap., xx, 473, 1919.
Crohn, B. B. Arch. Int. Med., xv, 581, 1915.
Culler, R. M. Journ. Am. Med. Ass., lxxv, 20, 1920.
Egdahl, A. Johns Hopkins Hosp. Bull., xviii, 130, 1907.
Farnam, L. W. Am. Journ. Med. Sc., clxiii, 859, 1922.
Finney, J. M. T. Ann. Surg., li, 818, 1910.
Fitz, R. Med. Rec., xxxv, 197, 225, 253, 1889.
Garrè. Beitr. z. klin. Chir., xlvi, 233, 1905.
Garrod, A. E., and Hurtley, W. H. Quart. Journ. Med., vi, 242, 1912.
Goebel, R. Arch. f. klin. Chir., lxxxiii, 784, 1907.
Gould, A. P. Lancet, ii, 1632, 1898.
Gross, O. Virchow's Arch. f. path. Anat., ccxxix, 90, 1920.
Guleke, N. Arch. f. klin. Chir., xcix, 120, 1912.
Heiberg, K. A. Die Krankheiten des Pankreas, Wiesbaden, 1914.
Heineke, H. Arch. f. klin. Chir., lxxxiv, 1112, 1907.
Hess, O. Medizinisch-naturwissenschaftliches Arch., i, 161, 1908.
Judd, E. S., and Mann, F. C. Surg., Gynec. & Obst., xxiv, 437, 1917.
Kehr, H. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xx, 45, 1909.
Kern, T., and Wiener, E. Deutsche med. Wchnschr., xxxix, 2085, 1913.
Körte, W. Ann. Surg., lv, 23, 1912; and numerous publications in German.
Lazarus, P. Ztschr. f. klin. Med., li, 95, 203, 521, 1904; lii, 381, 1904.
Lemoine, G. H., and Lapasset, F. Bull. et mém. Soc. méd. d. hôp. d. Paris, 3d Series, xxii, 640, 1905.
Link, G. Ann. Surg., liii, 768, 1911.
Mann, C. F., and Giordano, A. S. Arch. Surg., vi, 1, 1923.
Martina, A. Deutsche Ztschr. f. Chir., lxxxvii, 499, 1907.
Mayer, A. Ztschr. f. exper. Path. u. Therap., xx, 215, 1919.
Mayo, W. J. Am. Journ. Med. Sc., cxlvii, 469, 1914.

McClure, C. W., and Pratt, J. H. Arch. Int. Med., xix, 568, 1917.
Mikulicz, J. Ann. Surg., xxxviii, 1, 1903.
Miller, R., and Perkins, H. Quart. Journ. Med. xiv, 1, 1920.
Moffitt, H. C. Hare's Modern Treatment, ii, 371, Philadelphia, 1910.
Moutier, F. Ann. de méd., xii, 296, 1922.
Moynihan, B. G. A. Lancet, ii, 355, 1902.
Nordmann, O. Arch. f. klin. Chir., cii, 66, 1913.
Opie, E. L. Diseases of the Pancreas, 2d ed., Philadelphia, 1910.
——— Osler and McCrae, Modern Medicine, 2d ed., iii, 599, 1914.
Oser, L. Die Erkrankungen des Pankreas, Vienna, 1898. Trans. in Nothnagel's Encyclopedia of Practical Medicine, American ed.
Pemberton, R., and Sweet, J. E. Arch. Int. Med., i, 628, 1908.
Pförringer. Fortschr. a. d. Geb. d. Röntgenstrahlen, xix, 74, 1912.
Pratt, J. H. Diseases of the Pancreas, Oxford Medicine, iii, 473, New York, 1921.
——— Lamson, P. D., and Marks, H. K. Tr. Ass. Am. Physicians, xxiv, 266, 1909.
Rentoul, J. L. Brit. Med. Journ., ii, 1011, 1904.
Robson, A. W. M. Lancet, i, 913, 1904.
Robson, A. W. M., and Cammidge, P. J. The Pancreas, Its Surgery and Pathology, Philadelphia, 1907.
Schmidt, A. Deutsches Arch. f. klin. Med., lxxxvii, 456, 1906.
Sendler, P. Deutsche Ztschr. f. Chir., xliv, 329, 1896.
Simonin, J. Bull. et mém. Soc. méd. d. hôp. d. Paris, 3d Series, xx, 928, 1903.
Singer, G. Wien. klin. Wchnschr., xxxiii, 482, 1920.
Thomson. Cited by Robson and Cammidge, The Pancreas, Its Surgery and Pathology, 132.
Tileston, W. Arch. Int. Med., ix, 525, 1912.
Turner, G. Brit. Journ. Surg., vii, 394, 1919.
Villar, F. Chirurgie du Pancreas, 195, Paris, 1906.
Wallis, R. L. M. Quart. Journ. Mem., xiv, 37, 1920.
Walter-Sallis, J. Ann. d. dermat. et. syph., 5th Series, iv, 657, 1913.
Walters, W. Surg., Gynec. & Obst., xxxiii, 651, 1921.
Warthin, A. S. Tr. Ass. Am. Physicians, xxxi, 387, 1916.
Wile, U. J. Arch. Dermat. & Syph., iii, 122, 1921.
Wilms. München. med. Wchnschr., lxv, 204, 1918.
Wohlgemuth, J. Berl. klin. Wchnschr., xliv, 47, 1907; xlv, 389, 1908.

CHAPTER XXXIV

DISEASES OF THE PERITONEUM

JOHN T. HALSEY

ACUTE LOCALIZED PERITONITIS

Inasmuch as a localized peritonitis is almost always a secondary condition dependent on a primary diseased condition in a neighboring organ, the treatment of localized peritonitis is necessarily influenced by a consideration of the underlying cause. Therefore, a discussion of the treatment must be preceded by a brief consideration of the etiology.

Appendicitis and disease of the uterus and its adnexa are, by all means, the most frequent and most important causes of localized peritonitis. Ulcers of the stomach and in the large or small intestine, gall-bladder disease, inflammatory processes in or about the kidney, bladder, or prostate, abscess of the liver, pancreatitis, and intestinal obstruction are other common intra-abdominal causes, while disease of the vertebra or of the bones of the pelvic girdle and pleurisy may, at times, be the starting points of peritonitis. External violence, with or without rupture of an abdominal organ, may set up localized peritonitis. As a rule, peritonitis complicating acute infectious diseases is not localized, although at the start it may be so.

Prophylaxis.—The prophylaxis of localized peritonitis is of extreme importance and consists in the early recognition of the presence of any of the above-mentioned underlying conditions and the prompt institution of the correct treatment (often surgical), which has been discussed in the appropriate sections of this work. Often, however, the underlying condition gives no sufficient sign of its existence until after it has given rise to a localized peritonitis and, therefore, in such cases prophylactic measures cannot be observed.

TREATMENT

The chief aim of the medical attendant in a case of localized peritonitis should be the prevention of the spread of the inflammation into the general abdominal cavity. Much less important, though often not so

regarded by the patient or the physician, is the relief of the pain and other symptoms. It cannot be too strongly emphasized that a purely symptomatic treatment, carried out before any thorough attempt has been made to discover the underlying cause, is likely to be responsible for the evolution of a localized into a diffuse septic peritonitis, with its attendant grave prognosis. It is a rule to which there are few exceptions that morphin should be used not at all or very cautiously in the presence of localized peritonitis before the underlying cause has been carefully sought for and a diagnosis of reasonable probability reached.

Surgical Treatment.—The question of treatment, then, may be considered in the light of such diagnosis, and especially the question as to whether immediate surgical intervention is indicated or not. This will depend chiefly on the primary condition and cannot be considered here, as these conditions are so numerous, and as full discussions of the various indications are to be found elsewhere in this work. If there is evidence that the peritonitis is progressive, operative interference is usually indicated. A localization of the peritonitis is, however, not a contra-indication to operation, but this decision must depend on the underlying cause.

Medical Treatment.—If a decision against operation be reached, the so-called medical treatment should be instituted.

Rest.—An acute localized peritonitis demands that the patient remain absolutely at rest and in bed. All shifting and turning should be avoided except that indispensable to the proper examination and care of the patient. Bed-pan and urine bottle should be used, and the patient should not be allowed to raise himself to take food or drink, should such be allowed.

Relief of Pain.—The rest alone, with avoidance of any pressure on the painful areas, is at times sufficient to give marked relief, but usually we find it necessary to supplement this by other measures. The best of these is the continuous application of cold over the inflamed area by the use of ice bladders. In order to secure the best results from this procedure the application must be continuous. Attention must be paid here to three points. The ice-bags must not be so heavy as to cause pain or to oppress the patient, must be promptly refilled as soon as the ice is melted, and so applied and secured that they remain in the right place. This last appears so self-evident that it may appear superfluous to mention it, but frequent experience has shown that nurses, physicians, and patients are too often neglectful of this precaution. We cannot maintain with certainty that the external application of cold does more than relieve pain, but clinical experience gives some ground for belief that cold, if continuously applied, checks peristalsis and, in this or some other manner, favors a limitation of inflammation.

Penzoldt suggests that, though the ice-bag may have no direct influence on the inflammatory process, it renders valuable service by helping to

keep the patient quiet. It cannot be denied that there are patients who, even after a fair trial of sufficient duration, complain bitterly of the ice-bags, claiming that they not only do not diminish the pain, but that they increase it, or add to the general discomfort. In view of our uncertainty as to the real value of cold in these conditions, it is not advisable to persist in its use in such cases.

Hot applications may then be substituted.

In cases where the peritonitis is due to a lesion in the appendix or elsewhere in the alimentary canal, the author is averse to the use of heat externally, for there is good ground to believe that it stimulates peristalsis, which is not desirable in such cases.

It is often necessary to supplement the action of the local applications by pain-relieving drugs. Acetylsalicylic acid (aspirin) in doses of gm. 0.5 to 0.7 (gr. vii to x), or similar analgesic drugs, often act here most satisfactorily.[1] Opium or morphin, however, will often be indicated in spite of various disadvantages attendant on their use. From them we get most prompt and grateful relief of pain, and often, too, their power of checking peristalsis is of distinct benefit. On the other hand, the relief of pain may give a false sense of security to patient and physician, and lead to a failure to recognize unfavorable developments in the case, until valuable time may have been lost. Morphin should, therefore, be used cautiously, in as small amounts as will secure the desired relief, and the medical attendant should be on his guard against being misled by its masking of the symptoms.

The decision for or against its use and as to the dosage must be made in the individual case only after a careful weighing of these considerations, and it never should be given in amounts sufficient to stupefy the patient or to cause paresis of the bowel.

Diet.—In local peritonitis, due to appendicitis or other conditions in the alimentary canal, there is a general acceptance of Ochsner's view that neither food nor drink should be given by mouth, and that the stomach should be emptied by lavage. Any food or drink sets up peristalsis, and in these conditions we endeavor to avoid this. Thirst may be controlled by sucking of ice and by rectal administration of small amounts of saline, best given in the form of the Murphy drip.

In cases secondary to other primary causes such complete abstinence is not so urgently indicated, but the author believes that these cases will not be harmed and may be much benefited by following out Ochsner's plan. These patients are in no danger of starvation and will, at most, suffer only inconvenience by abstinence of several hours', or days', duration.

When the acute symptoms subside, easily digestible liquids and soft

[1] A combination of antipyrin, gm. 0.3 to 0.5 (gr. v to vii), with chloral, gm. 1.0 to 1.3 (gr. xv to xx), given orally or rectally, is often a very satisfactory substitute for morphin in these cases.

solids may be given in moderate amounts and, if well borne, a gradual return be made to the ordinary diet. It is best, as a rule, not to commence with oral administration of food or drink until the bowels have moved. If the need for food be pressing, a certain amount of food can be absorbed from the bowel. Grape sugar in 5 per cent solution is usually readily absorbed; 1,000 c.c. of such a solution contains about as much caloric energy as a glass of milk.

Bowels.—In the past there has been much diversity of opinion among physicians and surgeons as to the use of cathartics, but to-day all authorities agree with Ochsner in his strong condemnation of catharsis in any case of peritonitis where the appendix or other portion of the alimentary canal is involved. Until the condition has run its acute course, or has been relieved by operation, most authorities believe that catharsis is likely to have disastrous results, and they unite in recommending that the bowels be left undisturbed, or that, as occasion arises, they be cautiously moved by small enemata.

Even in peritonitis dependent on other causes the author believes this the preferable course, although many believe, with the late Lawson Tait, that free catharsis by means of the purgative salts exerts a markedly beneficial effect on the course of the peritonitis resulting from disease of the female genitalia. It may well be that in such cases the emptying of the bowel of its stagnating and presumably poisonous contents more than counterbalances any harm which may be done in the way of spreading the infection as a result of the active peristalsis.

Vomiting.—Vomiting, which not infrequently is a symptom in localized peritonitis, deserves our especial consideration as being often of grave significance, as well as being very distressing and harmful. Abstention from food and drink and lavage, repeated, if necessary, at intervals, are the best methods of treatment. Ice to the epigastrium and throat often aids, and morphin also will usually control it, at least temporarily. Persistent vomiting is a grave sign and, as a rule, is an indication for prompt surgical intervention.

General Measures.—Abundance of fresh air and a cheerful but quiet environment should, of course, be provided. The temperature and circulation rarely call for any treatment. When they do so, the indications are similar to those in general peritonitis, to the section on which the reader is referred.

Summary.—The cause of the local peritonitis should be determined and if this calls for surgical treatment this should promptly be instituted. Non-surgical treatment should always be conducted with the probable underlying cause in mind, with a careful avoidance of any procedures which could aggravate the primary condition. It consists, briefly, in absolute rest in bed, the continuous application of ice-bags over the inflamed area, and the cautious use of such drugs as acetylsalicylic acid

or morphin in doses just sufficient to ease the pain. In most cases no food or drink should be given by mouth, but fluid may, with advantage, be given by rectum. As a rule, catharsis is to be avoided, the bowels being moved by enemata. Vomiting is to be controlled by lavage, complete withholding of everything by mouth, and by the use of morphin.

ACUTE DIFFUSE PERITONITIS

(PROGRESSIVE SEPTIC PERITONITIS; ACUTE GENERAL PERITONITIS)

In the past over 90 per cent of these cases died, whether treated conservatively or surgically. To-day over 90 per cent should and do recover when the condition is recognized with reasonable promptness and immediately operated upon. Such results as these compel the conclusion that acute diffuse peritonitis is a surgical disease to be treated surgically. Only when consent for operation is refused, or where the underlying cause or the present condition of the patient is such as to indicate the uselessness of operative procedures, should the medical attendant content himself with non-surgical treatment. Absolute lack of the most rudimentary surgical facilities may, under exceptional conditions, also compel the physician to abstain from operation.

In addition to the etiological factors which have been enumerated in the preceding section, a general peritonitis may arise in the course of various diseases. Among these may be mentioned nephritis in its terminal stages, scarlatina, erysipelas, septicemia, and pneumonia.[2] The pneumococcus may at times, especially in children, cause a primary infection of the peritoneum.

Prophylaxis.—From a consideration of the etiology one must conclude that diffuse peritonitis is usually a preventable condition. Its prophylaxis consists in the prompt recognition of the conditions which may cause a peritonitis, and the institution of the correct treatment, which most often means prompt operation.

The author believes that most physicians and surgeons would concur in the estimate that, in an overwhelmingly large proportion of the cases of diffuse or general peritonitis which they see, early diagnosis and prompt and correct treatment would have prevented its development. The routine practice of treating cases of acute abdominal pain by a hypodermic of morphin and the administration of a purge is unfortunately apparently deeply rooted not only in the minds of the public at large, but also in those of a too large proportion of the medical profession. This procedure is

[2] See page 789.

undoubtedly chiefly responsible for a very large percentage of cases of general peritonitis and cannot be too strongly condemned. Fortunately the views of Ochsner and others as to the harmfulness of such treatment are now accepted by most surgeons and many physicians.

For further discussion of the prophylaxis of this condition the reader is referred to the article on the Treatment of Localized Peritonitis and to Ochsner's publications.

Treatment

Surgical Indications.—Once the diffuse peritonitis has developed, laparotomy should be promptly performed, and the necessary surgical work done as quickly as possible. The prognosis is so dependent on the time when the case is operated upon that the medical attendant should not hesitate to insist on laparotomy as soon as there is reasonable ground for suspecting the development of a diffuse peritonitis. Operation is contra-indicated in cases where the condition responsible for the peritonitis is of a character to make intervention hopeless. Such are, for example, cases in the terminal stage of nephritis, cases with severe diabetes, or cases of peritonitis caused by the rupture of an undoubtedly carcinomatous ulcer.

There is also a difference of opinion among the best authorities as to the advisability of operation in certain cases where the general peritonitis is of several days' duration and the patient's general condition extremely bad. It is most difficult to dogmatize here as to whether to operate or not. Undoubtedly there are certain of these patients in whom a laparotomy is likely to hasten death, or to destroy any chance of recovery which may remain. Further, we have all probably seen cases of general peritonitis go on to recovery after the surgeon had refused to operate on account of his conviction that the general condition was so bad that the patient could not rally after the laparotomy. Among those who advise waiting under such conditions are such leaders in surgery as Ochsner and Deaver, especially the former. Murphy and others of equal ability would appear to favor operation often in a certain proportion of those cases which others would consider unsuitable. In these apparently desperate cases the question for or against operation must be carefully weighed from all points of view.

The author must confess to an inability to recognize which of these cases will be given a better chance by failure to operate. His own position is that surgical measures give the majority of these cases their best chance to recover, and he, therefore, would advise operation in all cases in which the condition holds out a reasonable probability that they can survive a simple incision and drainage, which may be done under local or nitrous oxid anesthesia. The relief of tension thus obtained will, he believes, more

than counterbalance the harm done by the very small amount of surgical shock produced.

At times benefit is derived in such cases from the opening of a loop of gut and the insertion and retention of an umbrella catheter in this opening, which affords a channel through which flatus and stagnating feces may be passed and fluid or food be given.

Medical Treatment.—In those cases where, for one reason or another, a decision against operation is reached the so-called medical treatment must be carried out. Our indications here are mainly three: (1) the relief of pain and distress; (2) supporting the patient until such time as the disease may have run its course; and (3) an endeavor to diminish the toxemia which threatens to overwhelm the patient. It is, however, far easier to state these indications than it is to fulfill them successfully.

Rest.—Absolute rest as favoring the conservation of strength and the relief of pain is a generally accepted measure. The Fowler position has been of such value in the treatment of these cases after operation that it should be the one adopted. Whether it is of equal value in cases treated medically is questionable. However, in this position these patients are more comfortable. It mechanically facilitates the respiration, the passage of flatus or feces, and the oral administration of food, drink, or medicine. In addition, it is probable that, as a result of allowing the greater portion of the exudate to gravitate into the pelvis and away from the diaphragm, the absorption of poisons from the peritoneal cavity is retarded. All unnecessary turning or moving of the patient is most rigorously to be avoided.

Opium and Morphin.—Opium or morphin has always been our main reliance in these cases, and should be given regularly in amounts sufficient to relieve the patient's pain and distress, if this can be done without producing too great stupefaction and depression. By relief of pain and vomiting and securing quiet and rest this drug, more than any other measure, conserves the patient's strength. Its quieting of peristalsis is also, within certain limits, probably a valuable action. Lastly, in a disease of so nearly hopeless a nature, the relief of useless distress and suffering is by no means to be despised. On the other hand, their tendency to cause or aggravate paresis of the intestine is a most undesirable action of these drugs, as is also their power of later causing nausea and vomiting, an action too often forgotten.

Austin Flint advocated the use of opium regularly, persistently, and in large dosage (gm. 0.03, gr. ss, every three or four hours or more if necessary). He cites one patient who recovered after taking over 900 gr. of opium in one week. These large doses have fallen into disrepute of late years, but recently Stockton has urged the value of this method of treatment in cases not treated surgically.

The administration of opium in peritonitis was recommended by a number of observers: Watson, Graves, Stokes, and others. It remained for

Alonzo Clark to formulate a method for the application of opium or morphin, which has since been called Clark's method of treatment. In 1851 and 1852 this great clinical master treated the cases of puerperal fever in the lying-in wards of the old Bellevue Hospital of New York. As Alonzo Clark was in the habit of saying: a number of cases treated by him recovered, while without it practically all died. The method was originally employed in all kinds of peritonitis, notably by those who had come under the direct or indirect influence of Alonzo Clark's teachings. The puerperal cases were published, especially considered and referred to, because of Alonzo Clark's pathological views in connection with puerperal fever.

Opium or morphin was given in the following way. The first thing to be accomplished was the relief of pain; for an adult from ½ to 1 gr. of morphin, or its equivalent of opium, was given for this purpose. If the patient was not relieved in two or three hours another dose was given, smaller than the original one, provided the pain had been relieved. The pulse and relief of pain was the index of the dosage; the drug was ordinarily repeated every two to three hours. The production of undue narcotism was prevented by observing the pupils, the degree of somnolence, and the number of respirations. Alonzo Clark considered 10 respirations per minute as much reduction as was safe, although he often referred to 1 case in which the number of respirations was reduced to 6 and the patient recovered. As soon as respiration became too slow the dose was reduced and administered at longer intervals. One of Clark's cases took 1,018 gr. of opium in seven days—in the second twenty-four hours 472 gr. were administered, the patient recovering. The bowels were not interfered with; they were allowed to empty themselves spontaneously, which might not occur for a week or more; the utmost to be done was the use of a simple enema.

Diet.—These patients do not die of starvation. Vomiting is a very constant and distressing symptom and is only aggravated by attempts to give food or drink. Further, food is an exciter of peristalsis, which we wish to avoid. Early in the case, therefore, nothing should be given by mouth. After the more acute symptoms have subsided, liquid and semisolid food may be given and, if well borne, continued. If vomiting persists all oral administration should be discontinued. The need is for fluid, which can be best given in the form of a Murphy drip of hot saline to which dextrose 5 to 10 per cent and soda ½ to 2 per cent may be added if there be an urgent indication for nourishment. This has a certain food value, and is usually well absorbed.

Bowels.—Almost invariably a patient with general peritonitis becomes constipated and paresis of bowel and meteorism develop. This is a grave complication and one difficult to combat. If, by the cautious use of enemata and the passage of the rectal tube, we are able to mitigate this

condition, we are indeed fortunate. Should purgatives be used? Here is one of the most difficult of all points to decide. In the unoperated cases we are often in doubt as to what was the primary condition. If the case be one arising from appendicitis, obstruction, or perforation, and one which has not been operated upon, purgation can only aggravate the condition. If the general peritonitis be of other causation, the objections to catharsis are not so strong. In these latter cases the advantages of free purgation overbalance the probable disadvantages.[3] The ordinary cathartics frequently are ineffectual. Salines and calomel are, as a rule, the ones to be employed. In this connection it seems well to warn against the use of magnesium sulphate. Experience has taught us that in general peritonitis any cathartic may fail to produce an emptying of the bowel, and Boas has shown the danger of fatal poisoning which may result under these conditions. Sodium sulphate is equally efficacious and if absorbed is not poisonous. Eserin sulphate in doses of 1 to 1.5 mg. (gr. 1/60 to 1/40) hypodermically is frequently efficacious where other cathartics have failed. Of late surgeons have been employing pituitary extract as a means of moving the bowels in these cases. It is given hypodermically, 1 c.c.[4] (♏ xv) of the stronger (20 per cent) pituitrin at a time, and may be repeated at half-hour intervals. Turpentine stupes and other hot applications may relieve the meteorism.

Vomiting.—See article on Localized Peritonitis.

Temperature.—The temperature rarely calls for treatment. When it is high and continuous we must content ourselves with sponging with cool water or alcohol. This will rarely affect the temperature but will add to the patient's comfort. Antipyretic drugs should not be used.

Toxemia.—Toxemia, with its resulting depression of the circulation and respiration and of the central nervous system, is the cause of death in peritonitis, and urgently demands treatment. Evacuation of the bowels removes one of the sources of the toxic materials. The Murphy drip is the most efficacious means of lessening the harmful results of the various poisons. It should be started early and be almost constantly used up to the termination of the case. Experience has demonstrated its great value. At times intravenous administration of saline or hypodermoclysis will supplement or take the place of the Murphy drip. Caffein, strychnin, digitalis, alcohol, camphor, and epinephrin are all recommended as the drugs to be used in combating the general depression and especially that of the circulation. Of the digitalis group little can be expected. Strophanthin, mg. 0.5 to 1.0 (gr. 1/120 to 1/60), given intravenously once in twenty-four hours, should be the one used, but its value here is more

[3] It is to be emphasized that if the old Alonzo Clark opium treatment is employed no cathartics should be administered.

[4] The administration of a purgative enema immediately after the pituitrin has been given often aids in securing catharsis.

than doubtful. There is much diversity of opinion as to the value of strychnin. It may be tried, in dosage of mg. 1.5 to 2.0 (gr. 1/40 to 1/30) every two to four hours, until three or four doses have been given. If, then, no benefit is apparent it should be stopped, as in this dosage it is too poisonous a drug to continue.[5] Whisky, 15 c.c. (℥ss) every three or four hours, may also be tried. Its continuance or discontinuance should depend on its effect. The German school believes in camphor 1.0 c.c. (♏ xv) of a 5 per cent solution in sterile oil given hypodermically, but with us it is less favorably regarded.

The author formerly believed that caffein and epinephrin did good under these conditions, but his confidence therein has been greatly shaken in recent years. Caffein in the form of a strong infusion of coffee may be added to the Murphy drip or caffein and sodium benzoate may be given hypodermically, 0.12 to 0.18 gm. (gr. ii to iii) every two to four hours. Epinephrin may be given intravenously, 1.0 c.c. (♏ xv) of 1:1,000 solution to 500 c.c. of saline, introduced very slowly or intermittently, or it may be given intramuscularly, 1.0 c.c. (♏ xv) of 1:1,000 solution. As its effects are not lasting this must be repeated every hour. Its favorable temporary effects are at times unmistakable and it should be given a trial. Heat externally is one of our best stimulants. The author is convinced that he has seen striking benefit result from the use of an electric heating apparatus in cases with general peritonitis.

PNEUMOCOCCUS PERITONITIS

While there is a consensus of opinion that in the encysted forms of this disease prompt laparotomy and drainage result in the recovery of a large percentage (about 70 per cent) of the cases, there is much divergence of opinion as to the advisability of surgical intervention in cases where there is a diffuse peritonitis. In these cases Risbieth, Syms and others advise against operation and advocate treatment by Fowler's position, Murphy drip and morphin. On the other hand McCartney and Fraser and Gibson and Johnson, as a result of their clinical experience, advocate prompt laparotomy and drainage under nitrous oxid and oxygen or local anesthesia. The last-named authors, in addition to surgical intervention, suggest the use of antipneumococcus serum when Type I pneumococcus is the causative organism. As an additional reason for operation they point out that although before operation the peritonitis may appear to be caused by the pneumococcus there is always the possibility that explora-

[5] All experimental evidence with which the author is familiar fails to support the view that strychnin can be of value here, and some of it indicates that the only effects to be expected from it will be harmful rather than helpful. Personally he is against its employment.

tion may show such other cause as appendicitis and thus the operation may be a life-saving one.

TUBERCULOUS PERITONITIS

Surgical Versus Medical Results.—In the course of the last four decades our views of the prognosis of tuberculous peritonitis have undergone many changes. At one time regarded as a necessarily fatal disease and, therefore, as one in which treatment was only palliative, after König's communication in 1884, it was generally looked upon as a surgical disease with a relatively good prognosis if treated surgically. Surgeons reported numerous cases treated by laparotomy, claiming cures in a large majority of cases. Succeeding this wave of optimism, however, a change of opinion occurred, partly as a result of numerous reports of cures in cases treated non-surgically, but especially from investigation of the later history of the cases reported as cures following laparotomy. Among the first to call in question the value of the surgical treatment of this condition Borchgrevink, Wunderlich, and Rose should be especially mentioned. Especially important was the communication of Wunderlich, who, in 1900, analyzed the results of 344 cases treated surgically by various surgeons. Of these 344 patients, only 176 could be traced after three years, and of these only 46, or 26 per cent, were in good health. Of the 168 untraced cases, probably a still smaller percentage would have been found alive and well. Of more recent articles on the subject those of Stone and Hamman show that the permanency of the operative cures is far less than had been hoped. Cornet, in a review of nearly 1,000 cases, concluded that after laparotomy the percentage of cures was under 25 per cent, while Bircher gave the following figures for 1,295 operative cases collected from the literature: Immediate cures, 69 per cent; of these, 888 cases followed for one year or more, 31 per cent cures, while 634 cases which could be traced after two years or longer had elapsed showed but 28 per cent still in good health. The same author collected 600 cases treated conservatively with between 40 and 50 per cent of immediate cures and between 20 and 30 per cent of permanent cures.

In considering these results, one must remember that, generally speaking, the cases treated surgically were of a more favorable class than those treated conservatively, for, especially of late years, surgeons have refused to operate on cases of tuberculous peritonitis with advanced tuberculosis in other parts of the body, and, as a rule, have operated only on the cases with serous exudate, that is, on those cases which have the better prognosis. As a result, the cases treated conservatively have often been those with relatively bad prognosis. This difference in the character of the cases treated surgically and conservatively will perhaps account in part for the

somewhat poorer results in the non-surgical series. On the other hand, in reviewing the literature one must be struck with the frequency with which cases treated unsuccessfully by internal measures have shortly after operation been strikingly improved. It is also probable that the percentage of permanent cures following laparotomy would have been larger had the laparotomy been followed by a sufficiently long treatment according to approved so-called internal methods.

Surgical Indications and Contra-indications.—It is probable that most modern authorities are in accord with the view that, as a rule, cases of peritoneal tuberculosis should at first be treated conservatively along the same lines as are followed in the treatment of tuberculosis of the other organs and that surgical treatment is to be instituted in ordinary cases only after the conservative treatment has failed, or in the presence of definite indications. Among these latter are the presence of definite, marked, and probably primary lesions, such as a tuberculous tube, appendix, or ulcer of the bowel, or the presence of an excessive amount of peritoneal effusion which does not yield to internal treatment, or some condition causing more or less complete obstruction of the bowel. Ulcerative cases and the dry forms of peritoneal peritonitis, as a rule, should not be treated surgically. The prognosis in these cases is especially bad, and in them surgical intervention appears, as a rule, to do more harm than good. Advanced tuberculous disease in other organs is usually an absolute contra-indication to laparotomy except in the presence of some urgent surgical indication.

Local or nitrous oxid anesthesia should be used for operations in all tuberculous cases as a precaution against lighting up or aggravating pulmonary lesions, which is a real danger if ether be used.

Medical Treatment.—As mentioned above, the non-surgical treatment of tuberculosis of the peritoneum is essentially that of any tuberculosis. Proper food, fresh air, rest, and general hygienic measures are the essentials.

Tuberculin.—Tuberculin has the same indications here as in other types of tuberculosis and good results have been reported from its use. The initial dose should be small, in doses from 1: 1,000 to 1: 500 mg. of old tuberculin, which should be gradually increased.

Autoserotherapy.—In view of the favorable results which have been reported from autoserotherapy in tuberculous pleurisy at one time it seemed probable that this method of treatment might be of value in tuberculous peritonitis and reports of such results were published. However, it would appear that this expectation has not been realized.

Treatment of the Effusion.—Very often the effusion commences to subside after the institution of the general treatment, but if it does not do so special measures must be adopted. While free purgation and strict

limitation of the intake of fluids might act favorably here, as in other cases of ascites, these are both measures which work irreparable injury in a tuberculous patient. They should, therefore, be used cautiously and judiciously if at all. Good results have been reported from a salt-free diet. Not much is to be hoped from the use of diuretics, but they may be tried. It is possible that mercury inunctions owe some of their repute to their diuretic effects. Tapping is generally discountenanced as liable to do more harm than good (Graser).[6] A persistence of any large effusion after fair trial of internal treatment is one of the indications for laparotomy.

Constipation.—The constipation is to be treated by proper diet, enemata, and cathartics, according to general rules. Constipation may be caused by a partially obstructive condition due to adhesions or to an appenticitis and here we may have the indication for operative interference.

X-ray Therapy.—Scattered through the literature of the last twenty years are a number of reports of cases of tubercular peritonitis in which treatment by Roentgen rays has been followed by prompt improvement and recovery. While as a rule the number of cases reported in the different communications is small, their total number is large enough to be significant. The largest series and most favorable results are reported by Bircher who has been one of the earliest and stanchest advocates of this method of treatment. In three-quarters of a series of 155 cases, about equally divided between the exudative serous and the plastic adhesive types, he claims that cures were obtained after three treatments given at intervals of from three to four weeks. Others were cured only after from four to ten treatments.

Among others recently reporting successful employment of this method are Eisen, Weil, and Stephan. The latter believes it is especially useful following the removal of tuberculous tubes and appendices or other local lesions. The published results certainly justify the conclusion that Roentgen therapy should be given a trial in cases not responding satisfactorily to the usual treatment.

Heliotherapy.—In a considerable number of cases benefit seems to have followed exposure of the abdomen to the direct rays of the sun or to the rays from various types of lamps. Especially striking is Armand-Delille's report of cure following daily exposure to the sun's rays of the whole body of a young woman with grave cachexia and ascites, in whom three laparotomies had previously been unattended by improvement. Among others Elliot has recently reported successful results from sun baths.

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[6] The author questions the correctness of this view and has not hesitated to tap very large and distressing effusions in a limited number of cases and has seen no apparent harm but only apparent benefit from so doing.

Summary.—Tuberculous peritonitis is always a disease demanding internal treatment and only under special conditions requiring surgical treatment. Non-operative treatment is, in general, the same as that for tuberculosis in other parts of the body and consists mainly in rest, proper food, fresh air, and general hygienic measures. Tuberculin is to be used in selected cases. Moderate purgation, restriction of the diet, and the use of the ordinary diuretics are of very doubtful efficiency. Laparotomy is indicated in the cases with serous effusion if, after several weeks of conservative treatment, satisfactory progress has not been made. Other indications for laparotomy are the presence of well-defined and probably primary foci in the tubes, or appendix, a localized ulcerative process, or some condition causing complete or partial obstruction of the bowel. Excessive ascites or the persistence of a considerable effusion are also frequently indications for laparotomy. The ulcerative forms and those without effusions are especially unsuitable for operation and should not be operated upon except in the presence of definite and well-defined indications. X-ray therapy is worthy of trial.

PERITONEAL ADHESIONS

Peritoneal adhesions are the result of former acute peritonitis or of trauma at the time of a laparotomy. Their development may to some extent be hindered or prevented by prompt diagnosis and treatment of peritonitis or its underlying causes. While operating, the surgeon, by attention to this matter, can do much by various procedures to lessen the liability to the formation of adhesions, but we are not yet in a position to prevent their occurrence entirely.

As a rule, peritoneal adhesions cause no symptoms and, therefore, call for no treatment. Not infrequently, however, they do cause disagreeable and serious symptoms which urgently demand relief. When, by causing obstruction, adhesions threaten the life of the patient prompt laparotomy is indicated, but, fortunately, the indication is rarely so urgent, as they usually simply cause pain or distress to a greater or less degree. Whether such cases should be treated surgically or not depends largely on the degree of distress or disability caused by them. Frequently purely symptomatic treatment suffices to carry the patient along for a period during which the adhesion is absorbed or stretched sufficiently to inhibit its harmful action, or for the organ or organs affected to accommodate themselves to the condition so that the annoying symptoms disappear. This possibility should lead one to adopt a waiting policy when confronted by a case with distressing but not dangerous symptoms, attributed to the presence of adhesions. During this time massage or local counterirritations may be prescribed and the case treated purely symptomatically.

A further ground for postponing operative interference in these cases is found in the experience that, after being broken up, these adhesions frequently recur. Kelly has reported a case laparotomized fourteen times for recurring adhesions but finally and permanently relieved. In spite of the uncertainty of the relief the distress caused by such adhesions is not infrequently so great as to justify operation. Especially is this so in cases with adhesions in the neighborhood of the gall-bladder and the pylorus. Here, too, the results of operative treatment are especially good. Again, in some cases where the adhesions are responsible for obstinate and grave constipation, relief can be obtained only by operation, at times with short-circuiting of the bowel.

CHRONIC PERITONITIS

Chronic peritonitis presents itself under two forms, for which the indications are different.

Localized Form.—The localized form with a localized progressive inflammation, with the production of new tissue, is almost invariably caused by disease in some abdominal organ. Its symptomatology is often practically the same as that of peritoneal adhesions with the important difference that there is much less probability that the symptoms caused will spontaneously subside. The treatment should be based on that of the underlying disease. Otherwise the indications are similar to those of peritoneal adhesions, to the section on which the reader is referred.

Generalized Form.—The clinical picture here resembles very closely that of a tuberculous peritonitis. In fact, many cases first diagnosed as chronic peritonitis ultimately prove to be tuberculous. Simple laparotomy and other surgical measures, including the Talma operation (Moynihan), prove here of no value. As this condition is often associated with syphilis, cardiac or arterial disease, these, if present, should be treated. The usual methods of relieving ascites by reduction of fluid intake, catharsis, and the use of diuretics, are indicated. Tapping, often very frequently repeated, is, as a rule, necessary. Moynihan has recommended the intraperitoneal injection of epinephrin, 1.0 c.c. of 1:1,000 solution. At times, obstruction of the bowel occurs in these cases and must be relieved surgically.

MALIGNANT DISEASE OF THE PERITONEUM

The only treatment which holds out any hope of cure is surgical. Almost invariably, however, the extent and distribution of the lesions are such as to defeat any attempts at radical extirpation. Our treatment must

be purely symptomatic. Tapping to relieve the effusion, which is often present, is indicated.

REFERENCES

Armand-Delille, P. F. Bull. et mém. Soc. méd. d. hôp. d. Paris., No. 29, xlv, 1921.

Bircher. Die chronische Bauchfelltuberculose und ihre Behandlung durch Roentgenstrahlen, Aarau, 1907.

——— Strahlentherapie, ii, 646, 1920.

Boas. Journ. Am. Med. Ass., lv, 2037, 1910.

Borchgrevink. Mitt. a. d. Grenzgeb. d. Med. u. Chir., vi, 434, 1900.

Cornet. Die Tuberculose, 1909.

Eisen, P. Am. Journ. Roentgenol., iv, 602-604, 1917.

Elliott, T. H. Canad. Med. Ass. Journ., vii, 420, 1917.

Flint, Austin. Practice of Medicine, 6th ed., 580, 1886.

Gibson, C. L., and Johnson, K. Surg. Clin. North America, i, 307, 1921.

Graser. Handb. d. ges. Therap., 4th ed., ii.

Hamman. Johns Hopkins Hosp. Bull., Sept., 1908.

Kelly. Abdom. Surg., ii, 461, 1914.

McCartney, J. E., and Fraser, J. Brit. Journ. Surg., ix, 479, 1922.

Ochsner. Clin. Surg., 146, 1902.

Penzoldt. Handb. d. ges. Therap., 4th ed., ii.

Rischbieth. Quart. Journ. Med., iv, 205, 1910.

Rose. Mitt. a. d. Grenzgeb., 1901.

Stephan, S. Monatschr. f. Geburtsh. u. Gynæk, liv, 314, 1921.

Stockton. Buff. Med. Journ., lxiii, 373.

Stone. Bost. Med. & Surg. Journ., i, 813, 1910.

Syms, P. Ann. Surg., lxvii, 263, 1918.

Weil, E. A. Paris méd., vii, 289, 1917.

DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS

CHAPTER XXXV

THE ANEMIAS

C. F. Martin [1]

INTRODUCTION

The rational therapy and prophylaxis of any given disease must naturally deal with the etiology, with the removal of the etiological factors, as well as with the alleviation of the various symptoms which, in the course of that disease, require special treatment. Some discussion of the etiological basis upon which a classification can be made is, therefore, in place here.

Unfortunately, in the case of many of the anemias the etiology is so obscure, and the varieties of the anemias so diverse, that a proper classification is quite impossible.

While many of the anemias, such as those following hemorrhage, have an obvious causation and produce their own spontaneous cure, yet many, especially of the severer form, have so complex or, at all events, so obscure an etiology, as to render rational therapeutics in many of these types extremely difficult, if not impossible.

A careful analysis of the abundant literature dealing with various forms of anemias shows all too conclusively that we are far from a satisfactory understanding of the subject.

The scientifically exact classification of the anemias must be left until further facts are evolved upon the origin of blood-cells, upon the relation of toxins to peripheral cells and to bone marrow functions, as well as upon the significance of the presence of various types of cells, both red and white, in the circulating blood and in the tissues.

In the present state of our knowledge it must be admitted that transitions of a qualitative and quantitative character occur in all varieties of anemias, from the mildest forms of either primary or secondary anemia to the severest and most fatal cases. In a broad general way one might say that the primary types are those in which the blood-forming organs

[1] The author wishes to acknowledge the very valuable assistance of Dr. Maude E. Abbott in the preparation of this and the following chapters.

are chiefly involved, in the absence of any obvious local or well defined cause elsewhere, while the secondary types are associated with apparent and serious lesions in the organs or tissues, or with known poisons in the system, one or all of which may lead to a secondary disturbance of those organs where new blood is generated. Any such statement, however, when subjected to more detailed analysis, leads to many sources of confusion.

Many questions arise in regard to the diagnosis of some of the more severe anemias. To what extent is the bone marrow really responsible for some of these grave varieties, for example, pernicious anemia? Is the marrow to be regarded as an organ with a definite function, even as is the heart, or is its disturbance but one of the factors concerned in every anemia?

To what degree, again, is the anemia directly due to changes in the peripheral circulation? Does the action of toxins produce an hemolysis, or do these toxins merely act on the regenerative function of the marrow and prevent here the formation of new blood elements?

Or, again, is there a combination of these two factors, peripheral hemolysis and defective hemopoiesis?

Do we imply in the term "anemia" changes occurring, too, in the leukocytes, or should the word anemia be confined to the diminution of red blood-cells and deficient hemoglobin?

Too much stress cannot be laid upon the fact that anemia in any form is merely a symptom secondary to some definite cause, be it known or otherwise, and the term "primary anemia," as applied to the cause, is a pure misnomer, to be used only as a convenience, or, if you will, a cloak to our ignorance, implying, as it does, that, in the present state of our knowledge, the anemia is often cryptogenetic.

The so-called addisonian idiopathic primary anemia is in no sense primary, any more than is that due to the Tænia bothriocephalus latus, for both are due to a definite toxic cause, in the first unknown, in the second well defined. Even then, where we have reasonably conclusive evidence that the primary seat of the lesion is in the functioning organ of the blood—the bone marrow—we must recognize that anemia is a symptom only, not a disease entity—just as a systolic murmur in mitral endocarditis is merely symptomatic of an underlying cause. Presumably the difference between primary and secondary types lies in the fact that, in the one, defective hemopoiesis is fundamental and, therefore, of so severe a character as to induce formation of abnormal and probably embryonic types of cells, while in the secondary variety the erythroregeneration is either of a different type or a milder degree, less fundamental changes in hemopoiesis resulting, and, therefore, cells less abnormal in type and fewer of the embryonic character appearing in the blood-stream.

As we will see later, the so-called primary blood disease, known as pernicious anemia, may be divided into two main types: the curable or so-

called phanerogenetic, that is, where a definite cause is known and can be removed (bothriogenetic anemia, for example), as opposed to the other type (Addison's) in which no cause can be defined, but where a definite clinical picture exists and the patient dies sooner or later from the malady, showing at the autopsy certain well-defined pathological changes.

Clinically, both these types show the same morphological blood picture, and the etiology is the differentiating picture.

In chlorosis, again, we have another so-called primary blood disease, which is easy of diagnosis after exclusion of all other possible causative factors, and by the blood examination. In its typical form it, too, though secondary to some cause as yet unknown, has its own peculiar symptom-complex, even as that in Addison's anemia.

The secondary anemias, so called, have an ever-varying blood picture, sometimes like that of pernicious anemia and sometimes that of chlorosis, more often like neither, and all transitions may exist showing various types of blood pictures. It is this variation which makes a classification so difficult, for only by a combination of all the features, etiological, clinical, and pathological, can we attain near to the diagnosis and hope to formulate a satisfactory idea—and even with all these facts we are all too often left so much in doubt that a perfectly accurate conclusion cannot be formed.

Certain fallacies exist and should be recognized in order to be refuted. In the first place, the morphological features in the blood are not so all-important as has hitherto been believed. Poikilocytosis, anisocytosis, polychromasia, basophilic granular changes, fragility, etc., have much less diagnostic significance than has usually been attached to them, and possess a general rather than a special significance.

Secondly, hydremia and anemia are not synonymous terms, and the former does not imply the sequence of the latter.

The toxins which circulate in the blood do not necessarily affect the corpuscles, and probably do not act on the blood in the peripheral circulation so much as primarily upon the regenerative powers of the marrow, and thus the injury to the functions of the marrow may be the sole cause of the peripheral changes.

Pappenheim divides the severe anemias which resemble the pernicious variety into two types: the cryptogenetic (where no known cause exists) and phanerogenetic (with obvious cause) pernicious anemia.

The cryptogenetic form of pernicious anemia he declared to be also secondary and probably toxic in origin, the result of some blood intoxication, that is, an intoxicative hemolysis, be this an erythrolytic blood poison or a hemolysis in the immunity sense. Hemolysis is first the result of hemintoxication, and then becomes the stimulus to regeneration in the bone marrow. In this sense Addison's anemia is not idiopathic myelopathic, but the myelopathy is also secondary as result of hemolysis.

Therefore, in his view the primary lesion is not disturbed and altered erythroblastic growth, but the disturbed, strong, and relatively increased erythroregeneration.

There is, then, no primary pernicious anemia, but merely cryptogenetic.

The aplastic type of pernicious anemia, in which no evidence of regeneration is found postmortem in the marrow, he explains also as belonging to the same category of secondary anemias, in the sense that the condition is due merely to an absolute loss of secondary regenerative power in the bone marrow, which has been totally destroyed by some all-powerful toxin.

In the same sense Ehrlich's megaloblasts do not mean primary defective blood formation, but rather an indication of disturbed and overstrained secondary regeneration. The greater number of megaloblasts, however, does not indicate a more grave prognosis necessarily, but merely a greater effort at regeneration. We have, then, not a new growth, but a mere metaplasia, the cells having a definite function, that is, regeneration under greater hemolysis. There are more and more immature cells entering the blood, until finally in the supreme effort at regeneration on the part of the marrow, embryonic types appear. Such, at all events, are Pappenheim's views as expressed in his recent contributions on this subject. His classification is worthy of presentation.

THE SECONDARY ANEMIAS

(All anemias are secondary to some etiological factor)

I. Primary hemotoxic, secondary myelopathic (primary increased hemolysis), increased but insufficient secondary hemopoiesis.

1. Traumatic or posthemorrhagic anemia.
2. Simple primary hemotoxic secondary anemia.

II. Primary hemotoxic, myelotoxic, so-called pernicious secondary anemia (primary increased hemolysis, with secondary regenerative myelopathy and simultaneously primary disturbance of hemopoiesis).

1. Cryptogenetic Biermer's anemia.
2. Phanerogenetic symptomatic pernicious anemia (from bothriocephalus, leukemia, carcinoma, etc.).

III. Primary myelophthisic, myelometaplastic, aplastic hypoplastic anemia (primary reduction of blood formation, followed by secondary increased hemolysis).

Pappenheim regards anemia in two ways: (1) pathological; (2) according to the nature of the causative agent.

On a pathological basis there are two main types: the first concerns only the blood; the second the formative tissues, the latter being due to the action of some poisoning, whether it be destructive or productive in action. He considers three types of stimuli: (1) mechanical; (2) toxic; (3) excitant of plastic processes. Every case of anemia belongs to one of these varieties. He does not recognize such a thing as "primary anemia," but regards the study of blood films very properly as the effort to find if there is evidence or not of degeneration in the blood or in the marrow, and if, on the other hand, there is any sign of regeneration. The regeneration may be due to functional or to cytoplastic processes. Defective regeneration simply means a weakness or paralysis of the marrow.

Among the evidences of degeneration are the following: poikilocytosis; anisocytosis; loss of hemoglobin; scantiness of platelets; lymphocytosis, and deviation of neutrophils to the right.

Evidences of regeneration are: polychromatophilia, basophilia, and the presence of various forms of nucleated red cells.

Every anemia falls into this scheme, and is classified according to this process; they occur in varying degree and in varying combination.

Naegeli, on the other hand, insists upon the importance of primary disease of bone marrow function, as distinguishing one type of anemias which he calls primary, because the important feature is the disturbance in the function of the bone marrow inducing essential changes in the blood. These changes are shown in the character of the cell in the circulating blood and are both qualitative and quantitative. Such primary anemias include chlorosis and Addison's anemia. In both of these he regards the bone marrow as primarily at fault, and so disturbed in function as to be unable to produce cells that are completely developed. Hence the appearance of many embryonic forms. In chlorosis the defective hemoglobin or defective staining reaction (*polychromasia*) indicates this tendency. In pernicious anemia the same defective power is seen in the presence of large red cells and megaloblasts, representing what may be called qualitative changes and embryonic types. Or else quantitative alterations may occur in the number and variety of the cells. To him the diagnosis of pernicious anemia is easy, the blood picture invariably determining the type by the character of the cells.

Naegeli distinguishes two great classes of anemias, the one primary myelogenetic including the two conditions, pernicious anemia and chlorosis, as above mentioned, the other secondary myelogenetic. In this latter group he includes all the anemias other than chlorosis and the pernicious form, all of which show a blood picture different from that of the primary group in that the new cells are of a less embryonic type, giving less evidence of primary disturbance of bone marrow function. To these secondary forms, which he describes as purely symptomatic in nature, he attaches as the etiological factor either some general malady or some disease

of other organs, which affects the bone marrow secondarily and induces the anemia. In these cases he thus assumes that the bone marrow is *not* the primary seat of disease. It is in this way, for example, that he explains the anemia in sepsis, puerperal fever, syphilis, malaria, cancer, nephritis, and the parasitic diseases.

Naegeli's classification is herewith appended:

Primary myelogenic—

Chlorosis (defective qualitative blood regeneration).

Pernicious anemia (defective qualitative and quantitative blood regeneration).

Secondary myelogenic, to be grouped merely according to known causes—

Hemorrhagic (traumatic, or associated with infections or chemical poisons, or malnutrition).

Infectious diseases (parasitic or toxic causes).

Cachectic conditions (with chronic infections and intoxications, cancer, nephritis, and starvation).

Chemicals [arsenic, mercury, lead, chlorid of potash (direct hemolysis), pyrodin].

These various causes may act singly or together, and include in the widest sense the terms "toxins" and "hemolysins."

This classification is, however, not quite logical, as Naegeli himself admits. All possible transitions in the degree of anemia may occur between the primary and secondary myelogenetic types, and, secondarily, in such grouping, etiological factors are necessarily somewhat confused with associated conditions. The extent to which some toxins may affect the bone marrow so that the embryonic blood picture is produced, while other toxins or the same toxins in other cases produce no such picture, is hard to determine or explain. Parasitic diseases, for instance, sometimes produce primary pernicious anemia, and sometimes this secondary myelogenetic variety (symptomatic anemia), the explanation being that in the first case the toxin produced by the parasite affects the bone marrow function severely, while in the second it acts only upon this to such an extent as to favor the more moderate blood changes. The same is true of some cases of puerperal anemia, syphilis, and carcinoma, in which the specific "pernicious" embryonic blood picture is seen instead of the appearances usually characteristic of a simple anemia developing in the course of these diseases. Thus it is impossible to separate these two forms of anemia from an etiological standpoint.

Naegeli's views coincide with those of Pappenheim, however, in one essential feature, namely, that, *whatever the result on the blood or the blood-forming organs, there is some primary toxic cause at work.*

Lee and Minot adopt the following classification, which is, perhaps, the most practical and modern:

1. Anemia due to mechanical blood loss (acute and chronic).
2. Anemia due to defective blood formation. This includes anemia of cancer, tuberculosis, nephritis, etc.
3. Aplastic anemia and myeloplastic anemia.
4. Chlorosis.
5. Hemolytic anemias, for example, from chemical poisoning, acute infections, pregnancy, and certain cryptogenetic varieties. Under this heading are included splenic anemia, Banti's disease, Gaucher's disease and hemolytic jaundice.
6. Pernicious anemia. This may be acute or chronic, and recurrent over years.

For practical purposes we may conclude that anemia in whatever form is merely a symptom; that there is further a cause for every form of anemia that exists in disease, and that the cause is sometimes unknown and the condition called, therefore, cryptogenetic; at other times the cause is known and the anemia therefore is designated phanerogenetic.

It is the secondary forms which constitute by far the greater majority of all anemias, be the cause what it may, posthemorrhagic, traumatic, septic, toxic, or cachectic. These may be roughly classified into those due to definite blood loss and those due to toxic causes.

Posthemorrhagic Anemias.—Posthemorrhagic anemias typify those associated with blood loss. They may be acute or chronic, and recurrent over years, as in the case of uterine fibroids, hemorrhoids and duodenal ulcers. The anemia may be mild or severe, sometimes so severe as to simulate pernicious anemia; indeed, quite a few cases are recorded in which the typical pernicious variety seems to have followed the posthemorrhagic anemia.

Repeated bleedings, it is thought, may paralyze the functions of the blood-forming organs. After hemorrhage has occurred, however, increased coagulability soon takes place. The fine veins of the marrow are too small to allow a very hasty flow of blood, and thus the substitution of new blood is kept back. Oligemia occurs, but gradually is overcome by tissue fluid. The serum becomes more "watery," and hydremia results. The hemoglobin and red cells fall, but the index remains at 1.0. There is polynuclear leukopenia, and the platelets and reticulated red cells are diminished. Later, the marrow gives out new mature cells and regeneration begins. With severe hemorrhage and severe anemia one may get marked qualitative changes in the blood. There is an active polymorphonuclear leukocytosis, increase in platelets, and later, an increase in young red cells among which the reticulated variety are prominent. With repair the red cells return to normal much more rapidly than the hemoglobin, thus giving a low index and a chlorotic blood picture. The blood volume

is restored, resulting in dilution of both hemoglobin and corpuscles, till such time as regeneration is more advanced.

Toxic Anemias.—The toxic anemias arise from two sources:

1. Extraneous poisons of a chemical nature, inorganic and organic, produce anemias (for example, chlorate of potassium, anilins, benzol, pyrogallol, phenylhydrazin, etc.).

2. Autogenous poisons, formed within the organism as a result of different metabolic processes, likewise lead to anemia.

Combined Causes.—Many influences affect the blood through producing a state of lowered nutrition leading to defective hemopoiesis, and the anemias arising may be placed in the group of posthemorrhagic anemias as being caused by blood loss. Such, for example, are the effects of deficient light, of poor nourishment, of insufficient iron-containing food, and of too much food of a single variety, as, for instance, prolonged milk diet, all of which are accompanied by various forms of secondary anemia.

Many anemias arise partly from toxic causes, partly from bacterial or parasitic invasions, and some from this combined with hemorrhages of varying degrees.

All forms may be mild or severe, and often are transition types which merge insensibly into pernicious anemia. From a therapeutic standpoint, the severe secondary anemias call for remedial agents along the lines discussed in pernicious anemia.

Principles of Treatment.—The treatment varies according to the degree of blood loss. Minor hemorrhages are restored from tissue fluids, and no other treatment is necessary than rest, moderate warmth, good air and food. The larger blood losses become serious in proportion to the amount lost. As a rule, one may say that a loss of one-third of the total volume is fatal. In such cases, absolute rest is essential to prevent recurrence and to permit undisturbed recuperation. Hypodermic injections of morphin are usually beneficial. If possible, the cause must be dealt with and the primary disease treated.

Where a ruptured vessel is known to exist, it is sometimes well to leave it undisturbed, as, for example, in the gastric hemorrhages, which come on with sudden gushes of blood, and would seem to demand attention. The collapsed condition of the patient renders operative interference dangerous, and it is a wise practice to see what may be done first by means of transfusion to prepare the patient for splenic operation (see article on Transfusion—Pernicious Anemia).

Certainly, blood transfusion is often the means of saving life. The blood volume is restored, as also is the oxygen-carrying constituent.

1. Transfusion should be performed if the systolic blood-pressure falls to below 89-90 mm. Hg.

2. Where the blood loss is from 1 to 2 liters.

3. Where collapse is imminent.
4. Where the recuperative power of the patient is slow.

The amount of blood to be transfused should be large; 800 to 1,000 c.c. when the shock is great. On the other hand, if the transfusion is given for the purpose of speeding a convalescent period, small repeated transfusions are very effective.

Where a suitable donor is not available, one may use instead of blood an intravenous saline injection, with the addition of small doses of adrenalin chlorid, which ensures restoration of the blood volume. Gum acacia solution, given intravenously, has been found of even greater benefit than intravenous salines; it is more efficacious in maintaining the blood-pressure and its effects last longer than do the simple saline solutions.

The diet should be generous and nourishing. Evans concludes from experimental work on rabbits, dogs and cats, that the diet is of greater importance than drugs, and that meat is a necessity to rapid recovery. The use of the ordinary drugs recommended for anemias of several kinds seem of little avail. Musser was pessimistic on the use of iron in the hemolytic anemias. Arsenic and iron, on the other hand, have been recently insisted on by Aubertin. He points out that their respective actions differ in anemias. While arsenic induces new formation of red cells, the iron brings about hemoglobin formation and fixes it to the cells. Where then a combination of numerical and qualitative loss has occurred, the combined treatment is curative. As a rule, it is well to employ the two, not simultaneously, but in succession, beginning with the one most required according to blood findings.

Others have recommended doses of perchlorid of mercury, while for the debility phosphates are specially recommended. The bowels should be kept open, and in suitable cases massage and change of climate are worthy of consideration.

The efficacy of high altitudes for secondary anemias of certain kinds is too well known to need mention here.

Bickel recommends the use of thorium-X, especially in obscure secondary anemias of doubtful origin, and considers it the best remedy available for giving the initial impetus to an increased hemopoiesis. He cites a case of a girl, aged nineteen, in whom the red corpuscles numbered 1,700,000 and the hemoglobin was 45 per cent. Fifty thousand maché units were given intravenously, followed by 30,000 to 50,000 by mouth daily. The red corpuscles rose under this treatment in six weeks to 5,200,000, and the hemoglobin to 88 per cent. (For further details on treatment by radio-activity, see Pernicious Anemia.)

In the severe grades of chronic secondary anemia, there is great resemblance to ordinary anemia of the pernicious variety, and the therapeutics of the latter disease must be carefully followed.

CHLOROSIS

Chlorosis scarcely admits of a definition, for neither its immediate cause nor the pathological condition underlying its development is well understood. It presents, however, certain specific features which have been recognized ever since Vandeval first described it in 1620 (Stockman). It is a type of anemia coming on in girls or young women about the age of puberty, apparently of spontaneous development, and often appearing under good hygienic conditions. The most striking characteristic is a diminution of the hemoglobin normally present in the red cells, which may possibly be ascribed to an inefficiency of the blood vascular system showing itself under the exorbitant demands of puberty and the establishment of the menstrual period.

The subjects frequently show a family predisposition, and members of large families suffer more commonly than others. A first attack is said never to occur after the age of twenty-four, though relapses are frequent. The patients are usually well nourished, but present a characteristic pallor, which in extreme degrees is of the greenish hue from which the name is derived, and which is consistent in blond individuals with a bright red coloring of the malar eminences of striking contrast. They suffer from marked dyspnea on exertion and are quickly exhausted by slight effort, showing the need, too, of an abnormal amount of sleep, and in this way resemble early tuberculosis. In severe cases signs of slight cardiac dilatation, soft full pulse, venous stasis, and slight edema of the extremities appear. Digestive disturbances are common, but are not an essential part of the picture.

The blood examination shows only a slight reduction of the number of the red corpuscles, but a distinctly lowered hemoglobin content of the individual cells, so that the color index is reduced. The red cells also show a slight lessening in globular value, increased globular fragility, some polychromasia, and a lack of tendency to dispose themselves in rouleaux; there is relatively little poikilocytosis, as a rule, and nucleated reds are rare. The leukocytes are normal. The specific gravity of the blood is lowered both on account of the diminution of red cells and also because, according to Lorrain Smith, Haldane, and others, there is a marked increase of the plasma, and, therefore, of the total volume of the blood, a hydremic plethora existing.

Of complications occurring in chlorosis the most serious is venous thrombosis, with death from pulmonary embolism. Tragic deaths in chlorotic girls from thrombosis of the cerebral sinuses are also recorded, though, no doubt, quite rare. Few, if any, cases have come within the writer's knowledge.

Another and more frequent complication is gastric ulcer, which is so

often present that the association can hardly be considered accidental, and the question arises as to which of the two conditions is primary.

Chlorotic patients are also peculiarly susceptible to acute infections.

Most cases of severe chlorosis yield readily to proper treatment, the patient making a complete recovery in six to eight weeks. Relapses, however, are common, and are worse in the severe cases. Unfortunately they cannot be foretold, and if they occur year after year the prognosis must be guarded. The recurrence of a relapse may mean that the treatment was insufficient in previous attacks, and indicates the employment of more active measures. Some cases are obstinate, and there are habitual forms of chlorosis which give no sign of improvement in years. These are usually individuals of undeveloped vascular and sexual systems, in whom the disease has manifested itself unusually early in life, at the age of fourteen or earlier, and the prognosis is here bad. Perhaps these are not true chlorotics at all, as we understand the condition to-day, but the blood condition may be the effect of a true congenital hypoplasia of the blood vascular organs, under which picture the first cases of so-called chlorosis were described by Virchow.

General Treatment.—There is no question but that the specific feature of chlorosis is the reduced amount of hemoglobin in the red blood corpuscles, and that to restore the normal hemoglobin content of the blood, in other words to supply the iron required for the formation of the hemoglobin molecule, is practically to cure the condition.

Among the first to use iron in chlorosis were Sydenham and later Niemeyer, and since then it has come to be recognized as having a distinct specific action in this disease.

The question arises: Is medicinal iron necessary, or will rest, a diet rich in iron-containing foods, and mechanical therapy suffice for cure? Mild cases do well under such expectant treatment, the patient being put to bed or kept at rest in the sunshine and fresh air on a diet rich in iron and albumin, hydrotherapy, sweating, massage, etc., being employed to stimulate metabolism, and constipation being regulated, when necessary, by the free use of enemata of castor oil and glycerin (Ferreira). Severe cases, however, *need* medicinal iron, which alone produces marked progress. It must be combined with the above procedure to insure success, which is attained in all but a few intractable cases in one to two months.

Summary.—Severe cases require rest in bed, in open air, a diet rich in albuminous content, and easily assimilated. The alimentary canal requires special attention with a view to attaining as nearly as possible intestinal asepsis and regularity of evacuations. For this reason naphthol and cascara are recommended as a preliminary to the use of any hematonics. Iron in Blaud's pill is enough. Small doses will suffice and should be readministered over a long enough time (several months) in

order to obtain permanent results. Often it is wise to repeat a course of iron every few months.

The various therapeutic measures available must be severally considered.

Rest in Bed.—Confinement to bed until betterment is distinct (three to five weeks) is essential for all marked cases, especially for those with vascular symptoms. Even after the patient is allowed to go about, a rest in the early afternoon, and at other times during the day as well, must be enjoined. Abundance of fresh air and sunshine should be supplied. Under these conditions sleep is much better, and many complaints disappear quickly and forever. Even mild cases should begin treatment by a week's rest in bed, and then be made to rest much during the day and forbidden exertion of any kind.

Exercise is now known to be injurious in all degrees of chlorosis, for it implies muscular effort leading to the breaking up of the red corpuscles and to the waste of the hemoglobin which is so much needed by the patient; this is proved by the rapid exhaustion of these patients under relatively slight exertion, and by the early appearance of urobilin in the urine.

Food.—The importance of proper dietetic treatment cannot be overestimated, for the disease is primarily one of disordered nutrition. A generous diet rich in albuminous (iron-containing) material, such as meats, spinach, cream of beans or oats, fish, eggs, cream, etc., should be supplied. Raw meat, seasoned and given in sandwiches or minced, or as raw beef juice, is a valuable adjunct. Eggs in any form may be given for breakfast, and meat, roast or boiled, at the other two meals, with plenty of fruit and vegetables, chiefly of the green and less starchy varieties. Tea and coffee should be abstained from and water freely drunk. A light wine may be allowed at dinner.

The digestion of these patients varies and they suffer from dyspepsia. This must be treated in all cases by removing the cause, and by careful feeding, giving five small meals daily and nothing between. Milk should be taken in fair amounts, both for its nutrient value and because it is a diuretic and influences gastric acidity; if necessary it may be peptonized or diluted with limewater. If there be emaciation, fats, such as butter, cream, bacon, etc., should be given freely. An abnormal desire for abnormal articles of food is common to many chlorotics, and they will give preference at meals to olives, spices, pickles, sweets, etc., over food that is more nutritious. This idiosyncrasy is to be regarded more as a perverted taste than as a natural outcry on the part of the tissues for certain needs. Maillart's observations are of interest, inasmuch as he attributes the healthiness of the Genevese to the preponderance of vegetables in the diet and to the special Genevese stew of green vegetables. Essential anemias, he states, are rarely seen about Geneva.

Hydrotherapy.—This has been shown to be a most useful adjuvant in the treatment of chlorosis, promoting metabolism and soothing the nervous system. It is of benefit especially in the milder cases, and a number of instances of cure by the use of hydrotherapy and hygienic measures alone are recorded, no medicinal iron being employed (Armbrust). The observations favorable to this method indicate that real benefit occurs in a short time, the red cells increase in number, and the percentage of hemoglobin becomes greater; still, one can scarcely credit the rapid improvements in these, half an hour after treatment, which some writers, such as Winternitz, would have us believe occur. To be of use the measures employed must be fairly active, and their effect must be carefully watched and the treatment arrested if unfavorable symptoms, such as palpitation, etc., develop.

Hydrotherapy may be applied in various ways, cold, heat, diaphoresis, and combinations of these.

Cold Hydrotherapy.—There is little doubt that in many patients the administration of cold baths in various ways has the effect of a powerful tonic, and stimulates cellular metabolism, acting on the nerve endings and the cardiovascular system, and more or less directly improving the blood itself. Friction of the skin helps this action, for the circulation is mechanically stimulated and stasis and ischemia disappear, while organic oxidation increases. In using cold hydrotherapy it is doubtless best to begin with warm water and then to proceed from milder to severer measures. The treatment is best given in the early morning and should be preceded half an hour beforehand by a glass of warm milk, a cup of tea, or a little whisky.

The different methods employed are sponging, rapid cold immersion, friction with or without salt rubs, wet sheets, douche, cold sitz bath, carbonic acid bath, etc.

The *cold sitz bath* lasts from one to three minutes, and the abdomen should be rubbed by the attendant during the bath.

Friction is applied with the patient in bed, and it may be dry or wet. Winternitz's method of applying wet friction is to cover the patient, who is stripped of clothing, with a sheet, placing one arm wrapped in a towel wrung out of cold water outside the sheet. Rub through the wet towel, and follow by a vigorous dry rub. The extremities and body are treated thus in turn. Salt water may be substituted for fresh where special stimulating action is desired.

The *wet sheet* is applied with the patient standing erect. The sheet, wrung out of cold water, is wrapped about the body, beginning over the chest, descending under the left armpit, and then around the back and over the right shoulder and across the chest again to the left armpit. The sheet being thus held in position, rapid and vigorous friction is applied through it by an attendant, the flat of one hand being in front and

the other at the back of the patient. This is followed by a vigorous dry rub.

Such treatment should be followed by rest or exercise, according to the individual case.

Hot Hydrotherapy.—Hot baths are recommended by Matthes and others. Rosin suggests baths at 40° C. for fifteen minutes, followed twenty minutes later by cold, very rapid douche, then rest in bed an hour.

Diaphoresis.—Sweat baths are good where they can be borne, but it must be remembered that the treatment is somewhat depressing. They act upon metabolism and get rid of the excessive plasma in the tissues. The methods employed are dry or moist warm packs, hot air baths, electric light baths, until free perspiration results. As Wandel has shown, these *Schwitzkuren* need something else to raise the hemoglobin of the blood, and they are, therefore, best combined with iron medication. The processes involved in diaphoresis help the iron to circulate and to become transformed into hemoglobin. This reflection applies to a greater or less extent to all the processes of hydrotherapy.

Intestinal Antisepsis.—The obscure nature of chlorosis and its supposed toxic origin have led many physicians to believe that some form of auto-intoxication from the intestinal canal is responsible for the onset of this malady. For this reason intestinal antiseptics—so called—have been used, and at times with some apparent benefit. Of course the use of any safe antiseptic medication for the alimentary canal is more or less without any marked diminution of the so-called septic state, but in a mild degree the use of such drugs as salol and β-naphthol seems to render the stools freer from bacteria, of a better odor, and less putrefactive in character. That they are any the less "septic" on that account is difficult to say, but that they are less likely to cause "auto-intoxication" is a fairly reasonable supposition. The presence of constipation in chlorosis likewise lends some color to this view, and it is certainly our experience that a preliminary preparation of the alimentary tract is of use before commencing the iron treatment. For this purpose, in addition to purgation, we use frequently β-naphthol in 5-gr. doses three times daily for a week before giving iron in any form.

Iron.—The fact that iron cures chlorosis is well recognized, but the mechanism of its action is still unknown. Where in the organism is iron lacking? Is its diminution in the red corpuscle due to a defect of absorption in the stomach and intestines, or to insufficient assimilation in the cell itself? The supply of iron in the food is ordinarily quite sufficient for the hemoglobin, and chlorotics absorb all this food about as well as the normal individual. Why then, in severe cases, are the iron salts contained in the food insufficient for cure, even though a diet rich in proteins be given? And why is medicinal iron in addition necessary? Is medicinal iron absorbed by the gastric and intestinal mucosa, or does it produce

its effects by acting locally within these viscera? Replies to these questions and many others of a like nature still remain largely problematical, in spite of the large amount of experimental work which has been done.

It is the consensus of opinion that the defect seems rather to be due to lack of assimilation in the red corpuscle at the place of formation in the bone marrow than to faulty absorption from the alimentary canal, and that the medicinal iron acts favorably by direct stimulation of the bone marrow to increased hemopoiesis. Certainly, no proof exists of the presence of intestinal disorder of any marked degree, or of non-absorption. The ingenious hypothesis of Bunge that inorganic iron could not combine in the organism to form the hemoglobin molecule, and that medicinal iron was not absorbed by the intestinal wall, but acted by remaining in the intestine and combining with the sulphurated hydrogen and other bodies there, thus leaving the organic iron of the food free for absorption, has been now fairly disproved. The fact that chlorosis can be treated successfully by subcutaneouse injections of inorganic iron argues against the first point, and, secondly, it is now known that both organic and inorganic iron compounds are perfectly absorbed in the intestinal canal and carried by the blood and by way of the liver to the hemopoietic organs, where they are stored up as reserve iron, or are used at once, if needed, to form hemoglobin. These iron depots keep their iron content until the reduction of the hemoglobin in the red cells demands a fresh supply, when the reserve iron is transformed from its loose combination (ferratin) into the more stable hemoglobin (Erich Meyer).

The fact that the giving of iron cures the malady implies the entrance of iron into the hemoglobin molecules. The old theory was that the curative action of iron took place by this simple chemical process. It is now known, however, that its effects are more complex, and are general rather than local. This is borne out by the fact that under treatment the red corpuscles are first increased while the hemoglobin lags behind, the color index remaining low for a long time.

Von Noorden held that the iron when administered stimulated in some specific way the germinating capacity of the blood-forming organs, especially the bone marrow, and this is the generally accepted view, although sufficient proof has not yet been accumulated. This view is supported by several recent contributions. Hoffmann and Muller found experimentally that the bone marrow of animals fed upon iron, after having been artificially rendered anemic, was much redder and richer in erythroblasts than that of the control animals. Schmincke made a careful comparative estimation of the total erythrocyte mass, number of red corpuscles, and hemoglobin content, before, during, and after iron administration. He found, in the 12 cases investigated, an increase in the total mass of erythrocytes and in the number of red corpuscles, while the hemoglobin rose more slowly, especially at first. This he regarded as conclusive evidence of the

theory that iron, by stimulating the essential elements in the bone marrow, leads first to increased hemopoiesis and only secondarily, and much later, to a rise in hemoglobin of the individual corpuscle.

Morawitz and Zahn observed 38 cases with all the signs of chlorosis, in whom there was no deficit of hemoglobin, and gave them iron, in all cases with benefit, even when the general régime was not altered in any way. These cases, then, they considered were only pseudochlorotics, and yet iron did them good, from which they concluded it to be unlikely that either the theory of cure by simple chemical process or von Noorden's theory of hemopoietic stimulation covers the ground entirely. The evidence is scarcely sufficient to allow us to recognize as a special entity pseudochlorosis of the type described by these authors, for the symptoms of secondary chlorotic anemia are present in many forms of obscure infection and intoxication without the blood picture, making it probable that these cases of Morawitz and Zahn belong to this category.

Morawitz and Zahn maintain that the results of experiments on animals which are fed with a limited amount of iron and are then benefited by the use of metallic iron do not constitute an argument in support of von Noorden's theory. Of course, such animals are benefited, but the important thing is to see whether anemic animals to whom sufficient iron food is given are in any way influenced by the addition of the iron metal, that is, whether the blood formation itself is increased by these means apart from the improvement of the general condition. For this purpose they took a series of 24 rabbits which had been bled. In 12 cases iron was administered (liq. ferri alb. per os, or fer. cit. subcutaneously, in amounts equivalent to 0.003 gm. metallic iron daily). The other 12 cases received no iron. No difference was observed in the two series as regards blood regeneration, and they therefore concluded that iron does not work on these organs at all, but that its action upon metabolism must be general.

Such experiments, however, are not altogether convincing—quite apart from the fact that the metabolism of herbivorous animals is not necessarily analogous to that of man, and that the administration of iron to man is certainly followed by increased regeneration.

The action of iron in the body is probably of a complex nature. It stimulates hemopoiesis and stores iron for absorption. Whether it has in addition a direct chemical action upon the hemoglobin molecule, or a general action within the organism, other than the stimulation of hemopoiesis, as Morawitz and Zahn suggest, is not clear.

Van Gieson studied iron metabolism. He concluded that the old officinal preparations produce hemoglobin far more effectually than do the modern proprietary compounds. The preparations he considers the best for therapeutic purposes are the ferrous carbonate, the soluble oxid with sugar, the double salts with vegetable acids, the ferric chlorid solutions

given in large quantities of milk. He lays stress upon the fact that in iron medication the question of defective metabolism is important. That is to say, where this exists, iron cannot be expected to give good results. Patients must, therefore, be individualized and prepared for the course of medicinal iron which is to be instituted; rest, massage, milk diet, intestinal antisepsis, as far as possible, are all means to this end.

Digestive troubles are no contra-indication to the use of iron, but in severe indigestion it is well to precede the administration of the drug by the treatment of the gastric disorders, and then to begin by small doses, gradually increasing and decreasing again before discontinuing.

There is no need of large doses of iron, but to be effectual the treatment must be carried on until recovery is well established. "Relapses" often mean insufficient cure. The form of iron most commonly employed is the simple pilula Blaud (ferrous carbonate), giving one pill three times daily (that is, 7½ gr., 0.5 gm.) the first week; two pills three times a day (15 gr., 1.0 gm.) during the second week; and three pills three times a day (22.5 gr., 1.50 gm., in the day) until the hemoglobin content of the blood is normal, then *gradually* reduce. Care must be taken that the pills are fresh, so that the iron is given as the true ferrous carbonate, and not transformed into an irritant oxid. On account of its astringency, iron is hard upon the digestion and tends to constipation; it must, therefore, not be given to excess, or without due watch upon the bowel action. To obviate the latter difficulty it may be combined with cascara, aloes, or phenolphthalein.

If pilulæ Blaud disagree, ferric sulphate in 1-gr. pills three times daily may be used in the same manner as above, gradually increasing, or the dried sulphate, 5 gr., three times daily, but these forms are still more trying to the digestion than is the ferrous carbonate.

Vallet's pill is another good form of prescribing the ferrous carbonate. It differs from Blaud's pill in being made with sodium instead of potassium carbonate, and in containing licorice powder. It should be freshly prepared:

℞

Massæ ferri carb., 6.00 gm. (℥iss).
Pulv. glycerrhizæ, q. s.
M. fiat mass. Div. in pil. No. xxx.
Sig.—Three to five pills daily.

Tinctura ferri perchloridi, 10 to 30 ♏ (0.066 to 2.00 gm.) is good when anorexia is present. It should be given in a syrupy vehicle.

A prescription sometimes useful where other inorganic salts are not well borne is the following:

℞
Ferri sulphatis
Potassii carbonatis, āā 5.0 gm.
M. ft. pil. No. 100.
Sig.—One three times a day after food.

The milder compounds of iron, such as those with the vegetable acids or the saccharated carbonate, are suitable for children:

℞
Ferri carbonatis saccharati, 0.65 (gr. x).
Olei menthæ piperitæ, gtt. ii.
Pulveris cacao, 4.00 gm. (ʒi).
M. fiat pulv. Div. in chart No. xx (wax paper).
Sig.—One powder three to four times a day.

Or:

℞
Ferri iodidi saccharati, 0.1 gm. (gr. iss).
Sacchari, 0.3 gm. (gr. iv).
M. ft. pulv. No. i. Mitte tales No. 24.
Sig.—One to two powders daily.

Or:

℞
Syrupi ferri iodidi.
Syrupi simplicis, āā 50.0 gm. (ʒiss).
Sig.—One teaspoonful three times a day after food.

The hypodermic use of iron has long been in vogue in European clinics—the green citrate of iron, 1½ gr. (0.1 gm.), every second day.

Organic Iron Compounds.—It has been claimed that organic iron compounds have a distinct advantage over the inorganic salts in that they are more readily absorbed through the intestinal mucosa, and also that, being more closely allied to hemoglobin in chemical composition, they enter into their formation more readily. Oerum (Scandinavia) reports the results of experiments with organic and inorganic iron upon 12 rabbits and 10 dogs, which had been made iron-poor by repeated bleedings. He used hematin-albumin, ferratin, ferri sulphas, and ferri lactas, and found that, of all of these, hematin-albumin acted most quickly in restoring the hemoglobin content. He concluded that both organic and inorganic compounds are absorbed and are stored up in the body as reserve iron in two different forms; but that the latter is of use only in stimulating the organism to the formation of new blood-cells, whereas organic iron acts directly by entering into combination to form new hemoglobin molecules.

This conclusion, however, disagrees with the facts experienced in chlorosis, for tinctura ferri perchloridi quickly raises the hemoglobin content and improvement is rapid (E. Meyer). As a matter of fact, no form of iron is directly absorbed and transformed into hemoglobin, but all forms pass through the liver first, such as ferratin. Organic preparations have probably little real advantage over the inorganic compounds, except insofar as they are somewhat less irritant to the digestive tract, and perhaps contain food values of another variety. But there is already so much iron nucleo-albumin in the food that the further addition of so-called organic iron over the inorganic variety is of questionable benefit.

Various forms of organic iron are recommended by different authorities.

Iron somatose (Matzer) in doses of from 3 to 10 gm., in milk, bouillon, or beer, has given good results, so also *triferrin* (Kraus), a combination with paranucleinic acid, and containing 22 per cent metallic iron and 2.5 per cent phosphorus.

Ferratin was originally prepared by Schmiedeberg from pigs' liver and is now made artificially; it is tasteless and easily administered, but is probably not superior to inorganic iron.

Hemoptan (Clemm) is a mixture of blood and malt in equal parts, thickened in an air-free space. The hemoglobin and serum form easily soluble combinations with sugar, the blood albumin being formed into a saccharate which is a blood-colored, dry, crystalline, sterile preparation, containing animal iron, blood, salts, albumin, maltose, lecithin, etc., in easily assimilable form.

Euferrol (Hauschild) is a good preparation for weak stomachs. It is stable, not unpleasant, easily assimilated and retained. Given in capsules it has the essential constituents of Levico water. Its action is better when combined with arsenic.

Glavecke first used iron subcutaneously in 1883, employing ferratum citricum oxydatum, in which form the iron is not precipitated locally in the tissues, but passes quickly into the circulation (see Secondary Anemia).

Baths Containing Iron.—Certain alkaline mineral springs are particularly rich in iron, and these often have a remarkably good effect on chlorosis, especially when the water contains much free carbon dioxid, which produces a stimulating effect upon the skin, with redness and tingling, and thus helps the absorption of the metallic iron. The bath is often combined with the internal use of the water, about a pint being taken daily at first and larger quantities later. If the water be from a cold spring it should be warmed before drinking, as iron in cold water is more irritating to the digestion.

The cure may be carried out at home by substituting some of the alkaline waters rich in iron for those with carbon dioxid.

An interesting table showing the temperature and percentage of iron-carbonate or sulphate, alkaline salts, and free CO_2 contained in the various European and American mineral springs is given in Potter's translation of *Ortner's Treatment,* pages 164-165. St. Moritz and Tarasp, in Switzerland, Homburg and Schwalbach, in Germany, Marienbad and Franzensbad, in Austria, are all hot springs rich in iron and practically saturated with CO_2, and all except Schwalbach contain alkaline salts in addition. A number of alkaline chalybeate springs are scattered over the American continent. Among those so far analyzed the California Geysers, Sonoma County, California, and the Napa Soda Springs, California, are saturated with CO_2. Alkaline mineral springs containing iron with a relatively small amount of CO_2 are the Harbin Hot Springs, Lake County, Georgia; Indian Springs, Martin County, Indiana; Glen Springs, Schuyler County, New York; Bedford Springs, Bedford County, Pennsylvania; Hot Springs, Virginia, and many others.

Plasmatic Treatment of Chlorosis.—Robin and others regard these anemias as due to demineralization of the plasma and prescribe a saline solution followed by iron medication.

Arsenic.—Arsenic is a good adjuvant to iron, especially in cases where the red corpuscles are much diminished, showing that the bone marrow needs stimulation. Fowler's solution is the best preparation to use, though other varieties are also employed in chlorosis. It may be combined with iron as follows:

℞

Ac. arsenosi, gr. 1/60 (0.001 gm.).
Blaud mass., gr. x (0.65 gm.).
Ext. aloes. soc., gr. i (0.065 gm.).

M. ft. pil. No. i.
Sig.—One pill t. i. d. p. c.

Manganese.—It has been claimed that manganese or a combination of this drug with iron sometimes gives good results in the few cases in which iron fails.

Viccinimi investigated the use of albuminate of manganese in chlorotic women. He found it increased the hemoglobin and the number of red corpuscles, and that the increase persisted after the drug had been stopped, which was not the case with the other hematogenous metals; he concluded, therefore, that manganese was probably cumulative in action owing to its slow absorption. The elective action, he believes, therefore, to be deep, not superficial or transitory, and considers this action is evidently due to a direct combination with the molecule of hemoglobin, for the reaction of manganese is absent from the separated serum, while present in the blood-clot of the patient under treatment. It has also an indirect action by favoring oxygenation of the blood.

Cholesterin.—This has sometimes been found useful in chlorosis. Iscovesco's successful cases were chiefly of this disease. Dose—1 to 2 gr. (0.065-0.120 gm.) daily in pills.

Plasmotherapy.—The interesting results recorded by Piot of the action of hemoplase in chlorosis, as well as in other anemias, have been fully discussed in the section on Pernicious Anemia. It is claimed that hemoplase not only supplies the fluid containing the antibodies and other properties of the cell protoplasm, which may stimulate hemopoiesis, but also presents in an ideal form the iron constituents of the blood for subcutaneous use.

Serum Therapy.—Chlorotic patients have been successfully treated by the serum from sheep, into which 600 c.c. of anemic patient's serum had been repeatedly injected. Chloranemics improved, their red cells increased, and the color index was raised.

Treatment of Special Symptoms.—The digestive symptoms of chlorosis often predominate and render the recovery slow and unsatisfactory.

Anorexia is especially common, and is associated at times with gastric anacidity or hypochlorhydria. In such cases dilute hydrochloric acid is of benefit and may be best administered by adding 10 drops to a wineglass of water, sipping the mixture slowly after each meal. Sometimes pepsin is added to this, and though the scientific basis for such treatment is lacking, yet patients often affirm that its action is satisfactory. At other times stomachics and bitter tonics do good, and one may give with benefit gentian, etc.

Hyperacidity is even more common, according to Riegel, and when present is best treated with calcined magnesia, bismuth subcarbonate, and sodium bicarbonate, to which a few grains of taka-diastase may be added, thus:

℞

Bismuthi carbonatis.
Sodii bicarbonatis, āā gr. x (0.65 gm.).
Magnesii oxidi, gr. iii (0.25 gm.).
Pulveris taka-diastase, gr. ii (0.12 gm.).

M. ft. pulv. No. i.
Sig.—Three times a day, half an hour after food.

The bulk of the powder is an added benefit, as in all forms of hyperacidity.

Mineral waters are likewise commendable, especially the Carlsbad waters (Mühlbronnen), which should be given on an empty stomach.

In recent years, too, tincture of nux vomica in large doses, the so-called intensive treatment, has found favor in many hands, beginning with 10 gtt. three times a day after food, and going quickly up to 20, three times a day.

Others, again, praise the effects of olive oil, which, in the writer's experience, is most useful.

For gastrectasis, which is not common except in a mild degree, small meals are useful, and a wet Priessnitz compress night and morning; strychnin, where indicated, and, if ptosis be present, a suitable corset adjusted to exert pressure upward from the lower zone of the abdomen.

In all cases of chlorosis the diet is a source of difficulty, for, quite apart from digestive disturbances, there is often an unnatural craving for absurd and often non-nutritious foods, for example, sweets, spices (olives, pickles, etc.), coffee beans, cracked ice, wines, etc., and although it is the opinion of some authorities that this disease indicates a need of the organism which should be satisfied it seems to the writer more a perversion of the nervous system and indicates the need of psychotherapy.

In these cases some such dietary as the following may be advised: In the early morning weak tea with much milk, or else some orange juice, before the bath. For breakfast, eggs and bacon, weak tea, toast. At 11.00 A. M. some nourishing food or some small drink to stimulate the appetite—eggnog made up of half an egg and glass of milk—or else chicken broth, or sherry and egg, with a soda cracker or stale bread. The midday meal to consist of proteids and easily assimilated vegetables. At five o'clock weak tea and toast, or stewed fruits—and the evening meal to consist of light food with beef, ham, game, etc.

For the constipation mild purgatives such as cascara, phenolphthalein, or aloes may be used. Or the so-called phenolphthalated A. B. S. & C. pill.

℞

Aloini, gr. 1/6 (0.10 gm.).
Strychninæ sulphatis, gr. 1/60 (0.001 gm.).
Extracti belladonnæ, gr. ⅛ (0.008 gm.).
Extracti cascaræ, gr. ¼ (0.016 gm.).
Phenolphthaleini, gr. ¼ (0.016 gm.).

The nervous symptoms so often present in chlorosis need special attention. Fresh air, good food, and iron will do much to help these, but as so often happens there is perversion of the patient's "morale," and for this a judicious moral and mental discipline are needed and psychotherapy in its broadest sense should be employed.

For the neuralgias analgesics should be used with care. Local applications are best employed at first, a menthol plaster, and some counter-irritating ointment or liniment, for example, capsicin.

PERNICIOUS ANEMIA

In the treatment of pernicious anemia the first essential is a correct diagnosis. Much of the difference of opinion regarding the value of various forms of treatment has been in the past due to the wrong conception of what the term "pernicious anemia" implies or else to a faulty diagnosis. Even in the case of pernicious anemia described by F. Müller, in which the results of treatment are fully discussed, several occur in which insufficient evidence is afforded of the true nature of the disease, thus rendering a rational criticism of his method of treatment of less value.

Nägeli's view that the disease is essentially an affection of the marrow, and Morawitz's contention that it is hemolytic in nature, while the marrow changes are in the main reparatory in character, describe the opposing views on the etiology. A solution has as yet not been attained and no blood picture can be described as pathognomonic. Pappenheim holds with reason that there is no such thing as a "primary anemia." To him, pernicious anemia is merely a histohematological syndrome. The noxa, which sometimes has affinities for circulating cells and sometimes for formative tissues, is not always the same, and this explains the variations in the clinical picture. One studies blood films merely to find evidences of regeneration or degeneration. Defective regeneration means asthenia of the bone marrow. Clinically we do well to follow the broad classification into two types—those without known cause (Biermer's or Addison's cryptogenic anemia), and, secondly, those where the cause is known (phanerogenetic, or secondary, pernicious anemia), in which the blood picture is that of the idiopathic cryptogenetic type but the cause is clear.

Briefly, the symptoms are those of progressive general weakness, without noticeable emaciation, gradually increasing profound anemia, dyspnea, vertigo, slight edema of the subcutaneous tissues, palpitation of the heart increased on exertion, digestive disturbance with periodical attacks of diarrhea, general signs of indigestion, with nausea, frequently vomiting. Carr found an absence of hydrochloric acid in 53 out of 57 cases. It is essentially a hemolytic anemia, the cause being probably indirect. As a rule urobilinuria and stercobilin excess occur, and also a slight icterus. The spleen is usually enlarged due to one of two causes: either hyperfunction (hemolysis) or excess introduction of red cells. The hemolysis is further expressed by the varying degrees of hemosiderosis. It must be remembered that every pernicious anemia may go over into the aplastic form (absence of regenerative power).

Further, numbness and tingling in the extremities as a result of the involvement of the spinal cord, and tenderness over the long bones, due

no doubt to the changes in the marrow, form some of the important clinical features of the disease.

Remissions often lasting months and even years occur in the idiopathic type, though invariably after one or more relapses the patient gradually fails, dying from exhaustion or coma, or, more rarely, from hemorrhage of the mucous membranes.

The blood picture in its typical aspect has the following features: The red cells number less than 2,000,000, the color index is high, and the leukocyte count under the normal. Poikilocytosis is marked. Abnormally large red cells occur (megalocytes), with polychromatophilia, and there are many nucleated forms of varying size (megaloblasts, normoblasts).

The blood platelets are usually diminished. Frequently cells are common and are easily seen in the fresh smear. Another feature of importance is the immature red cell, which, when stained with brilliant cresyl blue, will show the reticulation appearance. When many of a small size are found, it is some indication of marrow activity; when larger cells of this type occur, the significance is less. Of the leukocytes the polynuclear forms are relatively diminished and the lymphocytes correspondingly increased.

In the remissions the blood picture may almost resume the normal or assume the characters of a secondary anemia from other causes.

General Treatment.—Medical science has of late years paid much attention to the treatment of pernicious anemia, and many new views have been formulated to aid in the methods of alleviation. No means, however, have yet been found that indicate any decided progress in minimizing the ultimate gravity of the prognosis. Remissions have been lengthened and life prolonged, but no records of permanent cures occur. There are those who believe that cures would be less rare were the patients to come earlier for treatment. Be this as it may, and it certainly does seem to be of importance to begin the cure as soon as possible, it does not seem to ensure complete recovery.

It is of prime importance to make an early diagnosis; in this way the possible "secondary" nature of the disease may be discovered, and a radical removal of the cause may end in ultimate relief. In the purely idiopathic cases, where no cause is found, one may say that no successful treatment can be foretold. What is beneficial in one case seems to avail little in another.

General Outlines of Treatment.—1. Rest is an essential, and where the signs are at all well marked and fatigue easily induced, the patient should remain in bed, or at least in the recumbent position, avoiding undue exertion.

2. Warmth is important, and to this end the use of flannel gowns should be advised, while fresh air and sunshine, and a salubrious climate,

are of undoubted benefit. In all varieties of cases, high altitudes are apparently contra-indicated.

3. Once the patient is placed at rest, a thorough search for possible sources of infection should be instituted. This ensures a thorough investigation of the teeth (X-ray pictures), the gums for pyorrhea, the sinuses, the gall-bladder, the genito-urinary tract, and the alimentary canal.

These having been excluded, or as the case may be, having been treated:

4. One should pay special attention to the diet.
5. Certain drugs are of benefit in alleviating certain symptoms.
6. Transfusion is of distinct benefit.
7. Splenectomy is to be advised under certain conditions.
8. Oxygen injections are sometimes given.
9. The use of the X-ray is recommended.
10. Other treatments have apparently less consequence, but will be mentioned seriatim (arsenic, salvarsan, etc.).

The care of the alimentary canal is of distinct importance. The mouth should be cleansed several times daily, and the teeth carefully attended to, not only in view of Hunter's theory that oral sepsis is the primary cause of disease, but that the appetite may be largely improved, and the patient's general nutrition better maintained. The alimentary canal is thus protected in part and secondary infections are to some extent avoided.

Diet.—No hard and fast rules can be laid down for the dieting, because of the well-known idiosyncrasies in regard to food to which these patients are liable. The more food that can be taken without causing indigestion and anorexia the better.

The food should be nicely served and given in small amounts frequently, and always as liberally as possible. For a fickle appetite milk and milk food with eggs, meat juice, and jellies are readily borne. Red bone marrow, fresh and uncooked, and served with pepper and salt, has been highly recommended, not as a specific, however, but merely as a food, and Croftan lays stress on the need of forced feeding with excess of albuminous foods, giving from five to six feedings in twenty-four hours, as well as rectal feedings of proteins twice daily.

Alcohol in the form of whisky, burgundy, claret, or hock may be taken in small quantities.

Grawitz has recommended a diet consisting chiefly of milk and vegetables, with lavage of the stomach every second day, and daily enemata, while by the mouth he gives arsenic and hydrochloric acid. This treatment, however, which deals in a general way with a disease for which the individual treatment is all-important, is scarcely worthy of serious consideration. Lavage of the stomach every second day, for example, has scarcely a rational basis, when we know of no condition in the gastric

mucosa that demands either washing out or stimulation. The atrophy of the gastric follicles, which is a degenerative process, and the consecutive absence of hydrochloric acid from the gastric juice would not seem to be easily influenced by internal hydrotherapy of this kind. While, on the other hand, the effort required to carry out this treatment is by no means trivial to a patient suffering from pernicious anemia.

Fenlon has suggested what seems to be a most useful diet for this disease, one which favors foods rich in iron to supply organic iron to the body. The diet is as follows:

1. Select foods high in iron, such as fresh fruits, green vegetables, eggs, cereals and meat.
2. Give 10 c.c. of one per cent hydrochloric acid after each meal.
3. With the absence of free hydrochloric acid in the stomach, restrict the use of meat to once a day. The meat should be run through a food chopper.
4. Allow 50 to 60 gm. of protein per day (about 1 gm. per kg. of body weight); the fat only, which is found in the foods; and from 225 to 300 gm. per day of carbohydrate (1,600 to 1,800 calories per day).
5. With the above low protein intake, select the complete proteins such as are found in eggs and milk or foods rich in nucleoprotein, as the livers of the various animals.
6. Avoid foods which may be irritating to the kidneys, such as prunes, cranberries, plums, grapes, etc., and excessive amounts of meats, meat gravies, coffee and tea.
7. Drink plenty of water between meals.

List of Foods Having High Iron Content.—Fresh apples, bananas, dates, figs, oranges, oatmeal, beef, spinach, radishes, celery, cauliflower, beet greens, corn meal, egg yolk, string beans, dandelion greens, tomatoes, carrots, strawberries, shredded wheat, liver, green corn, lettuce, cabbage, peas, canned and fresh peaches, pears, pineapple.

Typical Diet.—*Breakfast:* (*a*) Grapefruit, orange, banana, apple or apricots. (*b*) One egg. (*c*) Slice of toast. (*d*) Cornflakes, puffed rice, oatmeal, rice or shredded wheat biscuit. (*e*) Glass of skimmed milk. (*f*) Sugar as desired.

Dinner: (*a*) Potatoes, Irish or sweet. (*b*) One of the following vegetables: celery, cabbage or lettuce, peas (mashed or puréed), tomatoes, beets. (*c*) Slice of bread. (*d*) Glass of orange juice. (*e*) Two eggs or 50 gm. of liver, beef or chicken. (*f*) Desserts: baked apple, canned pears or peaches; salad of apple and celery; or pudding made of bread, rice or cornstarch. (*g*) Sugar as desired.

Supper: (*a*) Potato or macaroni. (*b*) Slice of bread or four crackers. (*c*) One of following vegetables: lima beans (puréed), tomatoes, asparagus or string beans. (*d*) Two egg yolks and one white. (*e*) One-quarter

glass of milk (*f*) Dessert: gelatin, fruit, tapioca pudding with fruit or rice custard.

Hydrochloric Acid.—The use of hydrochloric acid by mouth is found of distinct benefit, both to aid digestion and to prevent diarrhea. The absence of this ingredient from the gastric juice may or may not be a reason for its employment, but the practical results from its use have been witnessed time and again by the writer. We are in the habit of administering it in the form of from 5 to 10 drops in a wineglass of water, to be sipped during ten minutes after food, with the result that digestive disturbances often improve, food is better borne, and diarrhea often ceases.

Croftan reports brilliant results in several cases, and concludes that this treatment when supported by the ordinary hygienic measures, good feeding, etc., yields excellent results in about half the cases in which it is employed. Hess followed Croftan's procedure in 5 severe cases, with marked success in 3. Frequently in our own experience, hydrochloric acid alone has been followed by prolonged remissions, with return of the blood picture and general condition to a temporary normal state.

Oxygen.—Oxygen inhalations are, as a rule, useless.

X-ray.—The rationale is based on the theory that if splenectomy is beneficial, surely irradiation of the spleen should be of some use. Mosse, in a series of observations, has shown that proliferation of megaloblasts occurs as a result of X-ray treatment given over the long bones. Favorable results were shown by Hynek in 8 cases and by Rénon and Tixier in one case (combined with the use of diphtheria antitoxin), and definite improvement has followed some cases recorded by Jona. Patients receive from 6 to 12 treatments, just short of the erythema dose, at intervals of every few weeks.

Radium, Thorium-X, Actinium-X.—The peculiar properties possessed by metals of the radium group, of undergoing more or less rapid atomic disintegration with discharge of chemical energy, while emitting emanations consisting of rays of varying quality and penetrative power (alpha, gamma, and beta rays), lead to these substances a powerful biological action which is capable of direct therapeutic application. The discovery of radio-activity was followed by a wealth of literature and experimental work. As a result radium with its allies has been proved to have a definite effect upon the physiological processes of hemopoiesis, blood coagulation, blood-pressure, uric acid and general metabolism, and ferment activity. Conclusive clinical evidence is still wanting, however, as to its specific value in individual diseases.

In larger doses radium is an endothelial and general cellular poison. In smaller doses its effect upon the blood picture is *to produce a rise in the erythrocytes, which may amount later to a polycythemia,* and an early rise in the leukocytes with a later leukopenia.

Recently *thorium-X* and *actinium-X*, derivatives of the radio-active metals of the same name, have been employed instead of radium in internal medicine.

Thorium was first thought of as a possible therapeutic agent in 1898, when the radio-activity of its salts was discovered by Mme. Curie. In 1902 Professor Rutherford demonstrated that emanations similar to those of radium were given off by it and that these would render radio-active the walls of the container. Its remarkable effect in stimulating the formation of red blood corpuscles was next noted. These facts led Professor Bickel (1912) to try the action of thorium-X in pernicious anemia. His present method is to give 50,000 maché units once every four days intravenously until three doses are given, followed by 20,000 maché units daily by the mouth, the whole quantity divided into three parts, one of which is taken after each meal. The results were surprisingly good, only one case out of a number treated being unsuccessful. A typical case was that of a man, almost moribund, with red cells 960,000, Hb. 50 per cent; 50,000 maché units were given daily by the mouth for over ten months. In six weeks the blood picture became normal, erythrocytes, 4,610,000, Hb. 90 per cent, poikilocytosis gone. Six months later, in spite of persistent thorium treatment, a relapse occurred, the red cells falling to 2,080,000. Repeated improvements and relapses followed in spite of steady administration of thorium-X and cholesterin daily. The effects of thorium-X in pernicious anemia were thus seen to be transitory, but it was of value in restoring the patient to temporary health when other measures had failed. Bickel recommends it especially in the secondary anemias, where he believes thorium-X in small doses persisted in over a long period to be the best remedy known for giving the initial impetus to increased red cell formation.

Thorium-X has also been recommended by Arneth. In one case where arsenic had failed, repeated small doses of thorium-X (intravenously injected) produced a marked remission. Gradual increase in red cells and leukocytes followed, with a differential white count approaching the normal. Large doses are condemned. No claim is made by him for a cure of pernicious anemia by means of thorium-X.

Actinium-X has a remarkable degree of radio-activity, producing the shortest-lived emanations of all the radium elements. It sinks in 30 seconds to half its original volume, while radium emanations take a month and thorium ten minutes to fall 1 per cent. The therapeutic effect of this powerful substance has been made the subject of an elaborate study by Lazarus. After proving its relative harmlessness on himself and on animals experimentally, he proceeded to the treatment of various diseases, including one severe case of advanced *pernicious anemia*. The patient, a woman of fifty-one, had a blood count of 1,300,000, Hb. 32 per cent, marked poikilocytosis with many normoblasts and a relative

lymphocytosis. Arsenic, both subcutaneously and internally, had been tried without effect. Small doses, 20 to 30 electrostatic units (20,000 to 30,000 maché units), were given daily, divided into three parts, one part taken after each meal, with good effect, the red cells rising to 2,500,000, and the hemoglobin to 50 per cent.

The easy application of the form of radio-activity supplied by actinium- and thorium-X places it within the reach of the ordinary practitioner. In daily doses of 20 to 30 electrostatic units, divided into three parts and given after each meal, the treatment continued for from two to four weeks, it may be tried in all cases where irradiation is indicated, both as a supplementary measure and also especially where arsenic has failed, or is contra-indicated. Lazarus suggests combining the short-lived elements actinium-X and thorium-X with radium, thus obtaining together the intensity of action of the former and the lasting radio-active effects of the latter. (For therapeutics of radium see Chapter XXXVI, on Leukemia.)

Arsenic.—Byron Bramwell has very successfully studied the use of arsenic in pernicious anemia. In a large proportion of his patients marked improvement and, in many cases, temporary cures, resulted from this treatment, which was introduced by him in 1877.

The improvement under arsenic is greatest in the first attack and in cases in which the patient can take large doses; but in the majority of cases, notwithstanding the arsenical treatment, relapses occur and death ultimately takes place.

Arsenic, then, is sometimes useful, and at other times has no effect, and at other times again, while beneficial at first, soon loses its value. There are those (Gunn and Feltham) who think its action is protective to the red cells by being antihemolytic, as proved by its action on blood to which distilled water is added—the arsenic becomes rapidly united to the corpuscles and hemolysis does not take place. In *strong* doses, however, arsenic appears to be a poison of the blood, being destructive to it and to the hematopoietic organs, causing necrosis of these tissues, reducing the number of elements, and producing degenerative lesions with phenomena of the type of macrophage. This destruction gives way secondarily (in the case of acute intoxication) to a process of renovation. The red cells are increased and a mild myelemia takes place because of the reaction of normoblastic and neutrophil types in the marrow, followed by a mild reawakening of the myeloid activity of the spleen and glands.

In chronic intoxication both processes of destruction and repair evolve side by side. The anatomical features which present themselves are as follows: Destruction recognized by the ordinary phenomena of macrophage, sometimes resulting in pigmentary sclerosis in the spleen; regeneration with reaction in the marrow, and myeloid activity in the spleen and glands, and hyperplasia of splenoglandular follicles. The condition of the blood reflects the conflict of these two processes (Lefèvre).

Arsenic in medicinal doses, then, is not, properly speaking, hemolytic, but the contrary, for it ultimately excites hematopoiesis, acting similarly to the supposed good effects of the X-rays.

Varieties of Arsenic.—Fowler's solution is the form of arsenic most commonly employed in anemia, and is probably the most useful of all for routine administration. This consists of the liquor potassii arsenitis, containing 1 per cent of arsenious acid. It is usually administered in gradually increasing doses, beginning with 3 drops (0.18 c.c.) three times daily, and increasing 1 drop at each dose every third or fourth day until 20 to 30 drops (1.2 to 1.8 c.c.) are given in the day.

In France the *hypodermic* method is preferred. A combination is made of equal parts of the solutio potassii arsenitis, 1 per cent, and solutio sodii chlor., 1.33 per cent, and of this 6 to 20 drops are given daily for two weeks, followed by one week of abstinence.

Many other forms of arsenic are used, as the liquor arsenicalis hydrochloricus (dose 2 to 8 ♏, 0.12 to 0.48 c.c.), pilulæ arsenicalis, containing pure arsenious acid (gr. 1/60 to 1/20, 0.001 to 0.0032 gm.), etc., but it is questionable if any of the other varieties, including the organic compounds, are more beneficial than the old-fashioned Fowler's solution.

Organic Arsenic Compounds.—Various organic preparations, and especially the salts of cacodylic acid, have lately been much in vogue as being less toxic than metallic arsenic. Thus, when Fowler's solution is not well borne, one may use sodium cacodylate intramuscularly in doses of ½ to 3 gr. (0.03 to 0.20 gm.).

The organic compounds are best given subcutaneously, because, being taken up by the leukocytes and distributed directly to the tissues, they are probably less poisonous to the nerve centers than is metallic arsenic. When taken by the mouth organic arsenic is apt to be acted upon by reducing agents and broken up into metallic arsenic, and the advantage of the less toxic organic preparation is thus lost.

Among favorite salts of cacodylic acid recently recommended may be mentioned the *arsycodyle, neo-arsycodyle, ferricodyle, ferrocodyle,* and the disodium methylarsenate (arrhenal), all pure arsenic compounds containing 70 per cent of latent arsenic. The last-named arrhenal, "new cacodyle," is said not to be transformed into cacodyle oxid when taken by the stomach. The dose is ⅔ to 3 gr. (0.042 to 0.20 gm.) by mouth or hypodermically.

Arsenic, however, is apt to disagree in any form and must not be "pushed" without careful observation. This applies especially to the organic forms, for neither the degree of their relative toxicity nor the exact limit of their therapeutic dosage is as yet fully established.

The arylarsenates are aromatic salts of arsenic acid in which the organic radical that replaces hydroxyl in this acid consists of phenyl, toxyl, xylyl, or naphthyl. Of recent years the compounds atoxyl and

arsazetin, belonging to this group, have been claimed to have especial value.

Atoxyl (*sodii aminophenylarsonas or sodium arsanilate*) contains 27.2 per cent of arsenic. The dose by the mouth is ¾ to 3 gr. (0.05 to 0.20 gm.) daily for three weeks out of every four. It is best given, however, hypodermically, a 15 per cent to 20 per cent solution being employed; it should be freshly prepared with cold boiled water and should be slightly warmed before using to insure a complete solution of the drug. One begins by using 6 ♏ (0.35 c.c.) of the solution, increasing the dose each day until 5 gr. (0.30 gm.) of the drug is given daily, continuing this for four weeks, then reducing the number of injections to two a week, and then to one a week; then omit treatment for six to eight weeks.

It is said that atoxyl acts by primarily deoxygenating the tissues, thus leading to an increase in the blood elements, in a similar way as polycythemia occurs in high altitudes. It first destroys part of the blood, giving rise to acute deoxygenation, and this is followed by increased blood formation. It thus acts similarly to small repeated bleedings, and in the same way, too, as does tuberculin.[1]

Acetyl atoxyl or *arsacetin* (*sodium p-acetyl-amino-phenyl-arsinate.* Synonym: *sodium acetyl arsanilate*) is a still newer form of the arylarsonates than atoxyl, and one which seems to be a powerful agent for increasing blood formation, acting either by stimulating the bone marrow or by weakening disease agents. This discovery of Ehrlich's resulted from the unpleasant and even dangerous effects which atoxyl was known to produce in some cases, and which led to the attempt on his part to obtain a compound of similar action but of lower toxicity. As its name implies, arsazetin is atoxyl, with an acetyl radical added. It is a white, easily soluble powder which can be heated to 130° C. without decomposition, and can therefore be readily sterilized and resterilized, an immense advantage in hypodermic use. It has been proved experimentally to be much less toxic than atoxyl, and it is also relatively free from unpleasant effects. Such effects, however, sometimes do occur, especially in women, and the patient's tolerance should therefore first be tested by small doses. Optic atrophy occurred in a number of cases.

Klemperer described arsazetin treatment in 6 cases of pernicious anemia. Only 0.60 gm. (9 gr.) was used for two successive days each week, with remarkable results. The red cells rose at the rate of 200,000 to 500,000 per week, and in one patient from 440,000 to 2,320,000 in eight weeks, but in each case when 4.8 gm. had been used the good results ceased, that is, there was no further increase in the red cells.

We should not give too large doses of this drug, both on account of the

[1] Atoxyl has so frequently led to optic atrophy that the advisability of its use is decidedly questionable, particularly as many improved arsenical compounds are now available.—Editor.

untoward effect it may have, and because the results in anemia are thought to be better when it is given in small quantities. Neisser's directions, which were followed by Klemperer, are the best. He recommends 0.50 gm. (7½ gr.) given in heated solution hypodermically or by mouth. Then rest eight days and repeat until 4.8 gm. has been given.

Ehrlich, however, thinks arsazetin is no better than atoxyl for many diseases, while admitting that small doses of it seem to influence diseases of the blood favorably.

Salvarsan ("606").—Salvarsan is one of the most efficacious agents in the treatment of pernicious anemia, but like all other methods of treatment it is not curative—though it sometimes produces marked lengthening of remissions and rapid amelioration of symptoms. It appears to cause bone marrow reactions. Sometimes, as reported, there is a marked increase in the large mononuclear cells, as recorded by Evans. The dose is 0.3 to 0.6 gm. intramuscularly at intervals of days or weeks. B. Bramwell used it with success some years ago and more recently has favorably compared its use in 21 cases with that of Fowler's solution in former cases. There was no history of syphilis in the cases. Five of the cases were quite well some four years after treatment; 13 died from the disease. Hobhouse, Boggs, Leede, Maynard, and many others have recorded results with varying success.

Salvarsan rather than neosalvarsan is preferable. The drug is best given intramuscularly in order to obtain a more continued effect, and the dose at first should be 0.3 gm. repeated in a few days or a week and subsequently at intervals of one or two weeks for three or four doses. The results are usually reactionary at first—sometimes alarming—but soon the fever, etc., subsides and the patient begins to improve in a few days. The blood picture shows early improvement, the red cells may double and treble their number in a few weeks, the hemoglobin rapidly rises and the color index approaches the normal. Sometimes a temporary polycythemia picture appears.

It has been our experience at the Royal Victoria Hospital, Montreal, that while improvement occurs the blood picture never attains nearly the normal and that the subjective symptoms are the chief evidences of benefit. Relapses, too, are inevitable though often delayed for even years. No degree of severity contra-indicates its use intramuscularly. Certainly the salvarsan is directly responsible for amelioration in many cases though its mode of action is still unexplained. It is of use, too, apart from any history of syphilis.

On the other hand, one must remember too the frequent lengthening of remissions by other methods of treatment. In our own series of cases in Montreal one patient showed rapid and marked improvement with dilute HCl and no other drug, another one by rest out-of-doors, and a third, who had failed to respond to the usual forms of medication, finally devel-

oped almost a normal state of health (temporarily) from the encouragement derived by worship at the shrine of modern occultism.

Splenectomy.—Splenectomy is still being recommended in many quarters as the most modern and, perhaps, the most rational form of treatment. It has been practiced with increasing frequency during recent years, based upon the views of Eppinger and Decastello that the spleen has distinct hemolytic properties, and that its loss disturbs the metabolism and induces a nutritive stimulus to the bone marrow. Its removal was suggested by them, and the operation was performed with improvement in the symptoms. Experience has proved that splenectomy for ruptured spleen was sometimes followed by polycythemia, and this fact gave added impetus to the desire to remove the organ in pernicious anemia. The spleen, so to speak, bleeds into its own pulp because of anatomical changes in the vessel walls, and thus more and more red cells are destroyed by this hemolytic action. It has not, however, been successfully proven that this action does occur. It may be that the spleen is merely a depository for broken-down corpuscles, whose constituent elements are being worked over and prepared for use again in the body. However, it does not seem clear that splenectomy prevents the destruction of the feebly born red cells, which are formed in pernicious anemia and which are better than none, and, therefore, should be preserved.

Nevertheless, the marvelous results in many cases of hemolytic changes cured by splenectomy attest to the importance of this operation under certain conditions of hemolysis. Results are apparently most satisfactory where hemolysis is most active.

Another theory with which splenectomy is concerned is the disturbed function of the organ, or its hyperactivity. King, working out the metabolism of the lipoids, has found that splenectomy increases the total fats and cholesterins and diminishes the unsaturated fatty acids. These latter, however, are increased in the blood in pernicious anemia, and induce hemolysis; hence the benefits of splenectomy.

Roblee believes in the existence in pernicious anemia of a toxin related to the increase of unsaturated fatty acids, and argues that the spleen helps to elaborate these, and thus to diminish total fats and cholesterins which are antihemolytic, and that for this reason it should be removed. Ever since Eppinger's original suggestion in 1913, the literature has been replete with more or less commendation of the operative treatment of pernicious anemia. None, however, seem to claim more than an added period of remission, and admit likewise that its rationale is not fundamental. Klemperer and Hirschfeld report 6 cases (including 2 of Eppinger's) in which splenectomy was followed by marked improvement. In 2 of these the blood picture was promptly changed and the circulation was flooded with nucleated red cells suggesting regeneration.

Among many writers are Bruhn-Fahrous with 47 collected cases in 1912, and Krumbhaar with 153 cases; while Lee, Balfour, McClure and others reported success. So also did Huber (1 case), Jagic (3 cases), Vincent and Robertson (5 cases), and Griffin, whose cases numbered 53. Of these 5 were still living after more than four years, 3 lived for more than three years; mortality in hospital—5.6 per cent.

The chief feature of these results is that the total duration of the disease in 20 per cent of the cases was more than four years, while 10 per cent were living almost five years from the time of operation; in other words, life was definitely prolonged by the operation. Splenectomy, however, is not for every case, and doubtless of benefit only in selected cases, and to be done chiefly during periods of remission.

The same author, in conjunction with Szlapka, and later, Minot and Lee, is largely responsible for the revival of interest and confidence in the benefits of splenectomy. The striking effects in hemolytic jaundice are not repeated in pernicious anemia, it is true, but marked improvement does occur.

To summarize the results of the experiences of the various writers and those derived from the observations of our own cases, we may say:

1. That it is a fairly safe operation is proved by the fact that in Giffin's series of 245 splenectomies for various diseases, the mortality was 10.6 per cent.

2. Splenectomy is merely a symptomatic treatment and is not curative. Improvement is more uniform than by any other method—75 per cent, but eventually the progress is unchanged, though, on an average, life is prolonged. It reduces red blood-cell destruction and increases the activity of the bone marrow.

3. Not only is it usually an easy and safe operation, but it gives mechanical relief where the spleen is so large as to cause discomfort.

4. The selection of cases for splenectomy should never be done as an emergency. It is, of course, a serious operation and needs deliberation. All foci of infection must first be removed. The best types are the early ones. The cases that drag along unchanged, thus presenting an active hemolysis, do especially well, that is, those with enlargement of the liver. Younger patients do better than the older ones.

5. The contra-indications, if any, and the occasions where operation is not liable to meet with success, are acute febrile cases and those in a chronic advanced stage with marked changes in the cord. The operation should not be done during the halfway progress of exacerbation, nor during the relapse or during a blood crisis. It is more successful during the stationary or improving periods. The results are questionable in those cases where hemoglobin is lower than 30 per cent and where persistent blasts are found in the blood. The aplastic types do not do well. Where

operations are tried on these desperate cases, it is well to transfuse first before the operation. Where repeated transfusions fail, splenectomy is inadvisable.

6. The results in favorable cases:

(*a*) Rapid recovery from immediate effects of operation.

(*b*) Rapid remissions with marked improvement over long periods of time.

(*c*) The benefits last longer than in transfusion; the remissions are more marked and the relapses are less severe. It is believed, too, that the cord changes progress less rapidly. Vogel and others have recommended *transfusion after splenectomy* as giving even better results than either operation alone.

Transfusion

Transfusion is by far the most important of all the methods of treatment, inasmuch as it not only gives the patient a sense of well-being but encourages remissions and prolongs life.

History.—Transfusion was apparently known to the Egyptians, and later to the Romans, but since then not much attention was paid to it until 1492, when the blood of three youths was transferred into Pope Innocent VIII, who, in spite of the treatment, died of pernicious anemia. Folli used the method in 1654, and Denys, physician to Louis XIV, used it as a life-saving method occasionally, although only with moderate success. Since that time, animal blood has been used from time to time, sometimes with good effect, but for many decades past the importance of transfusion seems to have been unrecognized by the medical world. In 1874, Boisnot used defibrinated blood intravenously in cases of severe hemorrhage with cure, and more recently the successes of Ewald in 1895, of Morawitz, Cahn, Schultz, and Crile, 1906, have reawakened interest in transfusion, more especially in the treatment of blood diseases, of shock and of hemorrhage.

Excellent historical accounts are given by McClure and Dunn, and also by Ravdin and Glenn. In the latter history of transfusion, the names of Landsteiner, Moss, Agote, Lewisohn, Jansky, as well as those of Lindemann, Unger and Levine, should be noted.

Explanation of the Objects and Benefits of Transfusion.—There have been various opinions as to whether transfusion is beneficial, and whether or not its employment has any effect other than that to be obtained either by salines or solutions of gum acacia.

Briefly, it may be said that the use of salines may be beneficial where some increase in the volume of blood is required, and where the effect required is only temporary. The use of gum acacia solution is somewhat superior to salines in that the increased volume of fluid obtained by these

injections intravenously is sustained for a longer period than by the use of some salines alone. Transfusion, on the other hand, does far more than merely increase the volume of blood, for this, after all, is but a temporary measure. The introduction of new blood into the circulation stimulates blood formation, for blood originates in the blood-forming organs. This can never be accomplished by a saline or by gum acacia. Transfusion provides morphological elements and the active principles from the donor, which not only improve the impaired metabolism of the recipient, but stimulate both his cells and the hematopoietic organs. Transfusion does not rejuvenate old organs, nor does it repair diseased tissues, but it affords them time to regain their loss, and it is a stimulus to their new growth.

There is some doubt as to the duration of its effect. It seems assured that the transfused cells remain a considerable time in the circulation. Krumbhaar, it is true, found that 1/10 of the cells in the circulating blood are destroyed daily, but Ashby concluded that transfused cells might sometimes live as long as forty days in the peripheral circulation.

The *limitations* of transfusion are these: It is not a panacea, and any cure of disease it may initiate is brought about indirectly by stimulation of the bone marrow and other blood-forming organs. It would be wrong to endeavor to arouse too great an enthusiasm about its use, though in suitable cases and properly applied, it is certainly of great benefit.

Blood Compatibility of Recipient and Donor.—Our studies in hematology and immunity have led to the important observations that blood of different species often varies to such an extent as to render indiscriminate transfusion of great danger to the recipient. In the human subject, moreover, the variations are such that without previous tests for the compatibility of the bloods of the recipient and donor respectively, it is impossible to guarantee the safety of the operation. Landsteiner, in 1900, first demonstrated the phenomenon of iso-agglutination in the mixing of bloods, that is, that the serum of some individuals, when mixed with the cells of others, brought about clumping of the cells. Later, in 1910, Moss and Jansky demonstrated that in human beings, the bloods might be reasonably classified into four groups; in other words, that the agglutination reaction of red cells and sera in human beings varies in four ways. Hence it is possible to establish four groups dependent on the compatibility of the blood in each instance. In adopting this grouping, we take it for granted that there are agglutinins in the sera, and receptors for these agglutinins in the corpuscles. These groups may be arranged in tabulated form as illustrated by the table on page 835.

Example: Cells of I are agglutinated by serum of II, III, IV, and so on.

According to Moss, there are three agglutinins, one for each of Groups II, III and IV. In this way, one may test out the groups of sera II and III for all persons.

		Sera			
		10%	40%	7%	43%
Cells	I	0	+	+	+
	II	0	0	+	+
	III	0	+	0	+
	IV	0	0	0	0

+ = agglutination

Moss' original contention has been doubted by Unger, as also by Dungan and Hirschfeld, who believe that instead of three, there are only two agglutinations. There seems to be no doubt, judging from the observations of Culpepper and Abelson that overlapping of groups is possible, and that this explains to some extent the reactions that often follow transfusions.

In testing for compatibility of bloods, various methods are used. In general, there are two things to be considered, namely, the agglutination of corpuscles and hemolysis. Two dangers must be avoided:

1. The donor's corpuscles must not be hemolyzed by the recipient's serum.

2. The donor's serum must not cause hemolysis of the recipient's corpuscles.

Where the donors are already on hand and their groups known, it is merely necessary to find if the recipient's blood corresponds according to the grouping shown in the table. For institutional purposes, as well as for all emergencies, it is well to have a supply of donors whose groups are known, and also to have stock tubes of sera of Groups II and III in sealed tubes, kept in the ice-box ready for use. Under such conditions, the sera may be kept for months.

Method of Testing for Groups.—Take a few drops of blood from the patient and place in a test tube containing 2 c.c. of a 1 per cent solution of citrate of sodium. Shake this and place a drop of the mixture on each of two coverslips; to the one drop, add a drop of serum of Group II; to the other, add a drop from the tube containing the serum of Group III. Invert these over a hollow slide, leave in the incubator for half an hour, and examine them. The group can then be easily ascertained.

If the patient's blood belongs to Group I, agglutination occurs in both sera.

If the patient's blood belongs to Group II, agglutination occurs in serum of Group III only.

If the patient's blood belongs to Group III, agglutination occurs in Group II only.

If the patient's blood belongs to Group IV, agglutination does not occur in either sera.

As regards the recipient's blood, patients of Group II can receive blood only from Groups II and IV. Patients of Group III can receive blood only from those of Groups III and IV. Patients of Group IV can receive blood only from Group IV.

With regard to the donors: Group I can give to Group I. Group II can give to Groups I and II. Group III can give to Groups I and III. Group IV—a universal donor. All doubtful donors are to be discarded. Modern students have demonstrated the fact that it is not wise to rely upon the group method of testing sera as suitable in every case to avoid the dangers of transfusion.

Selection of Donor.—It is more and more agreed that *the mere testing out of patients by the group method is not so reliable as a direct test of blood to blood to prove compatibility.* Severe reactions are sometimes apt to occur when, for example, one uses indiscriminately the universal donor (Group IV). For each transfusion, then, it is well to test directly the blood of the patient against that of the prospective donor. The prerequisites in the selection of a suitable donor, that is, with suitable blood, may be summarized as follows:

1. A healthy man, free from malaria, syphilis, any contagious disease or recent acute disease, hemophilia, diabetes, and cardiac disease. The Wassermann reaction should be negative. Patients with polycythemia are good donors, as are also those with essential hypertension, provided, of course, there be no evidence of nephritis or other disease. There seems little ground to believe that patients with polycythemia have any better blood than that of an ordinary individual.

2. One should test out the blood for its compatibility after each transfusion. The blood of a recipient may change after the first transfusion, rendering the donor's blood unsafe for second use.

3. One should especially avoid a donor whose cells are agglutinated by the patient's serum. On the other hand, the red cells of the recipient and the serum of the donor may show agglutination, but that does not necessarily imply incompatibility because the volume of blood of the recipient is so much greater than the serum of the donor that such effects are practically neutralized.

4. Groups are less distinct in children, and for this reason direct tests should always be employed. In most cases the mother's blood is compatible with that of her child. The agglutination test is the easier, simpler and quicker method.

The method adopted by Levine, of Montreal, which has been found most satisfactory, is as follows:

Four small test-tubes are used, two for the red cells of the recipient and donor, and two for the serum, the tubes to be labeled accordingly for donor and recipient. Into the two tubes which are to receive the red cells drop 1 c.c. of sodium citrate (2 per cent), and allow 2 drops of the donor's blood into one tube and the same quantity of the recipient's blood into the other. Into the other two tubes respectively, place 2 or 3 c.c. of blood from the donor and recipient to obtain the serum. The red cells must be washed with 5 c.c. of normal saline solution to get rid of the sodium citrate. This is done by gently shaking until thoroughly mixed; the blood is then centrifugalized, and the clear serum remains above, while the red cells are deposited at the bottom. Centrifugalization should free the serum from the clot. Next take two glass slides, and at each end place a ring of vaselin to support a coverglass. One end of the slide is marked "D" for the donor, and the other "R" for the recipient. Then add a few drops of saline to the tubes containing the red cells, so as to make a homogeneous mixture. With a clean pipet, take one drop from the tube containing the donor's red cells and put it into the circle marked "D" on the glass slide; with another clean pipet, take a drop of the red cell mixture from the recipient's tube, put it into the circle marked "R" on the glass slide. Next, to the circle "D," add a drop of the recipient's serum, and to the drop of red cells in circle "R" on the glass slide, add a drop of the donor's serum; mix well with a glass rod; place a coverslip on the vaselin circle and put in the incubator for one hour. If any agglutination is to take place, it will be shown microscopically by the cells appearing in clumps. *If at the end of an hour, or even half an hour, no clumping has taken place, the blood is fit for transfusion.*

Quick Method.—Levine also employs a much simpler method, more rapid, and, according to his own experience, quite as satisfactory. A drop of the donor's blood is placed in the tube with sodium citrate. In another tube, 1 c.c. of the recipient's blood is collected and centrifugalized for the serum. A drop of the serum is mixed with a drop of the donor's cells, and a tiny drop of this mixture is placed upon a coverslip in the circle by the hanging drop method. If agglutination is going to take place, it is very easily detected by the microscope. If present, the blood is not used for transfusion. If no agglutination takes place, this practically proves that the blood is satisfactory.

The possible influence of the type of donor, and the frequency of reactions in patients to whom he gives blood, has been investigated by Meleney, Stearns, Fortuine and Ferry. One donor, who was used sixteen times, gave to his recipients reactions on fourteen occasions; while another gave fifteen transfusions with only seven reactions. The largest number of donations made by one man was thirty-six with twenty-eight reactions.

There is thus a considerable difference between donors in their tendency to produce reactions. It is also thought by some authorities that certain diseases, such as pernicious anemia, present a special tendency to reaction no matter who the donor may be. This, however, is doubtful if, after each occasion, satisfactory tests have been made.

Indications for Transfusion.—Transfusion is of use in all cases where the blood supply has been depleted, and is, therefore, employed with satisfaction in primary hemorrhage, as well as in postoperative hemorrhages; also in hemorrhages following typhoid fever and in hemorrhage of the newborn. It is likewise useful in such cases where hemorrhage may be anticipated, and for that reason it was used very largely during the War in cases of shock accompanying wounds where operation was required. As a pre-operative measure, it is commendable wherever hemorrhage must be avoided. Satisfactory results have been recorded of cases with cholelithiasis and jaundice, where the pre-operative transfusion obviates the dangers of subsequent bleeding.

In blood diseases of various kinds, transfusion has met with unqualified success. This applies not only to the grave secondary anemias, but also to pernicious anemia, hemophilia, and purpura. So, too, in various forms of septicemia, more especially in puerperal septicemia, transfusion has been used with good effect, and more recently it has been recommended for generalized furunculosis, and for widespread burns. The results of transfusion in Banti's disease, which have been very striking, are referred to elsewhere.

To summarize the indications for transfusion, one may say that there are three types of cases in which this method is to be used:

1. Severe loss of blood from any cause.
2. In diseases of the blood, where it stimulates the hematopoietic function, increases coagulability, and increases the oxygen-carrying capacity of the blood.
3. It has, moreover, bactericidal and antitoxic properties, and hence it is useful in various forms of sepsis.

Transfusion is sometimes successfully used for cases of carbon monoxid gas poisoning, after a preliminary phlebotomy.

Dangers of Transfusion.—While it was Bernheim's impression that one was justified in giving blood transfusions without making agglutination tests, and while Berard, who did much transfusion during the World War, found not a single instance of trouble from those cases after many indiscriminate transfusions without tests, it is, nevertheless, true that the present method of testing compatibility is so simple and so rapid that one is scarcely justified in carrying out the operation without an effort to avoid what may be a considerable danger.

Much has been written of the dangers of transfusion. Blood is a

complex tissue, and the changes in its quantity and quality are numerous. The ideal to be attained is to give to the receiver a blood which is both potent and acceptable.

The chief dangers in transfusion arise from the effect, as Landois showed in 1875, of agglutination and hemolysis, which induce dangerous and often fatal reactions; and these, too, sometimes *in spite of* the fact that the pretransfusion tests for compatibility seem satisfactory. There is a special danger if the serum of the recipient agglutinates the cells of the donor. The danger of mixing non-homologous blood-sera is well illustrated in the case reported by Pepper and Nesbitt, where an obscure hemorrhagic state followed the transfusion, terminating fatally in a few days from intense hemolysis.

It is important to note that the first test of the blood may show compatibility, or only a very slight deviation from it, while in the next transfusion the same blood may be markedly incompatible. Or again, the bloods may even be compatible to the ordinary test, and hemolysis may yet occur, due to the production of new hemolysins or agglutinins.

The reactions that so frequently occur after transfusion are important. They may appear in one hour after the transfusion, or twenty-four hours later, or even longer, the danger symptoms indicating some form of protein intoxication. There is restlessness, nervousness and chilliness; there may even be a rigor with fever, increased pulse rate and dyspnea. There is often pain in the back, with nausea and vomiting; jaundice not infrequently follows, and hemoglobinuria occurs occasionally. Primrose records 2 such cases in 32 transfusions. As a rule, these reactions are followed by recovery; death is not frequent. A fatal termination, however, may occur suddenly, or within twenty-four hours after the transfusion has been carried out.

In general it may be said that the frequency of reactions cannot be sought for along the lines of one general cause. No doubt on some occasions defective technic produces the reaction. At other times, the contact of the donor's blood with foreign substances. No doubt immunology will at some future time explain the reactions in a satisfactory manner. The investigations of Sellards and Minot and others eliminate the theory that free hemoglobin in the blood is the main cause of reaction.

It is contended that reactions take place more commonly under the citrate method than under the transfusion of whole blood by the direct method. Whether or not it is so, it is quite certain that reactions follow either method, though statistics seem to show that they are most common when the blood has been altered by some anticoagulant. Thirty-five per cent of the cases in which citrated blood was used were followed by reactions, while only 15 per cent gave reactions where the direct method was used.

The records of Butsch and Ashby are of interest. Seven hundred and

thirty-seven transfusions were given by the citrate method. (*a*) It was found that the reactions were less marked when the patients had previously normal temperatures. (*b*) They were commoner if the hemoglobin was under 30 per cent. (*c*) The reactions had no relation to fasting. (*d*) They had no relation to the duration of the operation. (*e*) The reactions were less in proportion to the number of transfusions (an experience which differs from that of Bowcock). There is no doubt that the technic is of great importance.

Levine and Segall are of the opinion that reactions cannot all be accounted for by inaccuracy of tests for incompatibility, but that there are other conditions to be sought for in explaining their onset. In a very important work recently published, they have shown how, after the use of ether, the patient's serum may be so altered that its agglutination properties make transfusion difficult. They have frequently known in the serum of anesthetized patients a pinkish tinge after centrifugalization due to hemolysis of the red cells, most probably caused by the presence of ether in the blood. The same thing has been found by Bruère, of Montreal, in testing for the Wassermann reaction. The results are by no means reliable when the blood has been taken during or immediately after a prolonged ether anesthesia. Reactions following upon transfusion are extremely frequent, and are usually indicated by the presence of fever, chills and prostration, but in most cases these symptoms are ephemeral. More rarely hemoglobinuria may appear, and still more rarely, death follows upon the operation.

Bowcock's observations are of importance. He finds that repeated transfusion from the same donor resulted in severe reactions; in some cases there was hemolysis, and reactions occurred resembling anaphylactic shock. For this reason the rule has now been established that a second transfusion from the same donor invariably requires a new test for compatibility.

Other sources of danger arise from the technic of the operation. It is, of course, of great importance during the operation to avoid the admixture of any thromboplastin from the wounded tissues of the donor's vessels, as well as of the thromboplastin which might be derived from the cells of the blood through friction during the transfer. The dangers from air embolism seem much exaggerated; at all events, air purposely introduced into the veins of lower animals, during experimental transfusion, produced no serious result.

Dilatation of the heart as a result of transfusion is easily avoided by the modern methods employed to estimate the quantity of blood, and, secondly, by the proper selection of cases. Thus, for example, in pernicious anemia one should not use large quantities of blood where the heart is enfeebled; otherwise dilatation is almost certain to occur.

Quite recently Robertson and Rous have come to the conclusion that

in cases of repeated transfusion one should test for auto-agglutination in the recipient's blood, and they also point out that serum separated at 37° C. contains more agglutinins than that separated at room temperature; whereas agglutination is more marked at room temperature than at 37° C.

Technic of Transfusion.—Quite a number of methods are used. Briefly they fall into four groups:

1. Direct transfusion.
2. Transfusion of whole or unmodified blood.
3. Transfusion with citrated blood.
4. Transfusion by preserving the red blood corpuscles.

With the improvement in modern surgery and the additions of asepsis, the manipulation of blood-vessels in skilled hands has become a comparatively simple matter. Thanks to the genius of Carrel and Crile, a renewed appreciation of transfusion has gained ground. If to-day appeal is seldom made to their methods (artery to vein transfusion), we are, nevertheless, indebted to their zeal for making it more obvious that transfusion is not only a benefit, but is often a means of saving life.

It should not be supposed that transfusion from arteries to veins is by any means an obsolete method, for, during the recent crisis in France, such brilliant surgeons as Berard and Lumière employed the method with success. However, the necessity for skill in this method has given place to the simpler methods which are capable of use by any neophyte. Lindeman's method, which consisted in a vein-to-vein transfusion by means of a series of syringes, and which was successful, has now become obsolete except in children, where small amounts of whole blood are required.

Direct Method.—This consists in the transfusion of blood from the donor's veins directly into those of the recipient. The most modern technic employed in this method is that of Unger, and the modification by Levine of Montreal. In these methods the recipient and donor, whose bloods have been found compatible, are placed side by side (head to feet) on adjacent beds or tables, with a small table between to hold the apparatus. Their adjacent arms are placed close to the edge of the table, and prepared for the operation. A short needle attached to a rubber tube is placed in each of the veins of the recipient and donor; the two tubes are safely attached to a stopcock resting on the table, and are thus connected with syringes that alternately withdraw the blood from the donor and supply it to the recipient.

In Unger's method, saline is used to flush out the instruments, and ether is employed to keep the syringes cool. Levine does away with both. When a syringeful of blood has been withdrawn, the stopcock is turned, thus allowing the blood to be injected into the recipient. In this way, both channels are constantly suffused with blood and clotting is prevented. The apparatus is previously washed with a thin solution of paraffin, which

further prevents the clotting. In fact, Levine keeps his apparatus in a jar of sterile liquid paraffin. The method is rapid, from 30 to 60 c.c. of blood per minute being thus transfused. The speed may be controlled, and the blood is kept outside of the body for a minimum of time, so that clotting is in every way prevented. Unless the patient is very stout or the veins very small, there is no need to expose them as the needles may be inserted with ease directly into the veins through the skin.

Transfusion of Whole Blood.—This indirect method of transfusion is employed in various ways. Kimpton's method consists in the use of large paraffin-coated glass cylinders (250 cm.), with an exaggerated S-curve at one extremity drawn to a fine point, allowing its insertion into the veins. The blood is collected from the donor's vein and subsequently expelled into the recipient's vein by means of a rubber bulb. The paraffin coating delays coagulation and allows a reasonable interval to elapse before the blood is injected.

There are obvious disadvantages to this method, which has been replaced by others. It is not always easy to withdraw blood in this way from the donor's veins; moreover, accidental clotting if and when it occurs renders useless the large quantity of blood withdrawn. In skilled hands, however, this method seems to have found favor in some localities.

Citrate Method.—The citrate method of transfusion was apparently originated by Dr. Agote of the Argentine Republic. More publicity was given to it by the work of Lewisohn, and more recently George Miller strongly advocated the use of whole blood transfusions. He had already published his method in 1914. The transfusion was given by means of a record syringe (20 c.c.), attached to a shuttle and two canals, by which the blood was alternately connected with the donor's and recipient's veins. He transfused 257 patients with safety, and of this number only 3 suffered chill and 3 had febrile reactions.

Gravity Method.—The blood is collected from the donor in an open vessel containing citrate solution, 1 to 5 per cent, and 20 c.c. of this solution is used for 100 c.c. of blood. When properly mixed by stirring, the blood is transferred to another vessel, connected by a rubber tube to a needle in the recipient's vein. The donor is elevated, and the blood is allowed to flow in, just as one would use an intravenous apparatus. The objections to this method are: first, that one cannot control the injection; secondly, that one requires a long tube, which opens up the possibilities of infection and clotting; and thirdly, that the open method is in itself a source of infection.

Three-way Method with Syringe.—Two pieces of rubber tubing are connected with a 50 c.c. rubber syringe by means of a Y-tube of glass, or three-way stopcock. The free end of one tube is inserted in the flask of citrate fluid, while the free end of the other is connected with a needle inserted in the recipient's vein. The objections to this method are that of

contamination; that it is clumsy and requires several assistants; that there is long tubing with the apparatus; that leakage and plugging may

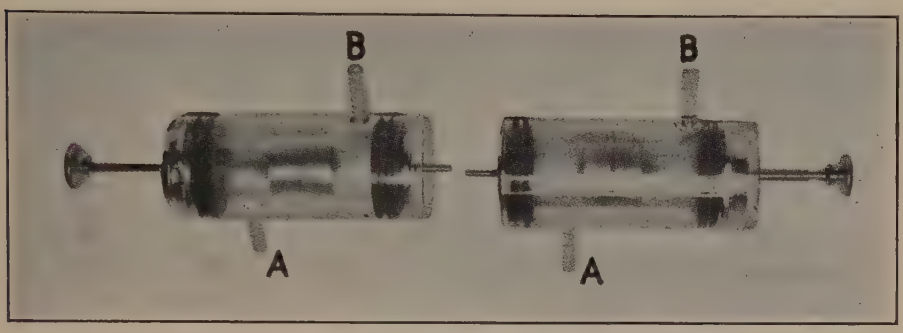

FIG. 1.—LEVINE'S APPARATUS. Syringes with jackets.

occur; that the plunger is liable to stick; and, lastly, that the red cells being forced, break down with resulting reactions. With regard to the donor, in this method it is important to get the pressure slightly lower than

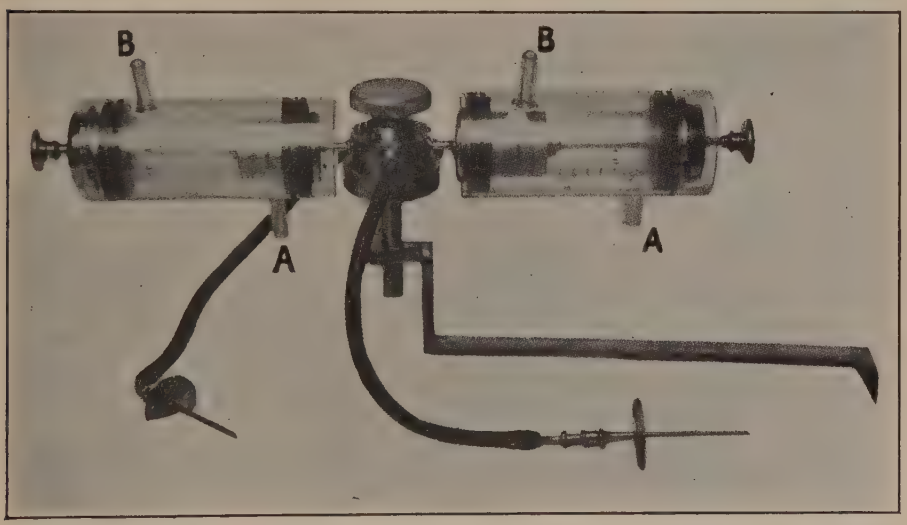

FIG. 2.—LEVINE'S APPARATUS. Illustration shows intake A, connecting it up with a douche can filled with ice and water. Another tube attached to outlet B to carry the flow of water into a pail on the floor. The object of the cold water flowing over the syringe is to keep the steel plunger cool, which otherwise would become heated by coming in contact with the blood, and in expanding would jam the barrel of the syringe and prevent any quantity of blood being given.

the donor's diastolic pressure; this ensures one obtaining a maximum flow of blood.

Method of Hoffmann and Habein.—By this method the blood is withdrawn under gentle vacuum into a flask, and from the same flask is

propelled by the reverse action of the aspiration pump into the recipient's arm. The method is simple, safe, free from contamination, requires only one person to carry it out, and the other fluid is usually steady and uniform.

Transfusion in infants is usually done by the citrate method. The needle is inserted into the longitudinal sinus, and, as a rule, no ill effects should follow. Lowenberg reported 13 such transfusions, without any injurious results.

The use of defibrinated blood, which for a time found favor, has now become practically obsolete and need not be discussed. As a matter of fact, a number of authors have used this method with success, though for various reasons the technic has been superseded by those methods mentioned above. Hanssen transfused 26 cases, of which 15 were pernicious anemia, and 6 gave excellent results.

Quantity of Blood to be Removed from the Donor.—After removal of a certain quantity of blood, the volume is quickly restored in healthy people. One thousand c.c. removed may induce lassitude for a few days, but not longer. One may easily remove 500 c.c. per week without causing discomfort or danger.

Quantity of Blood to be Given to the Recipient.—To replace the blood lost, from 600 to 1,000 c.c. should be used. To overcome toxemia, smaller amounts used frequently are in all probability better. For severe anemias, a larger amount given once is, as a rule, more effectual. One must remember, however, that a sudden increase of the blood volume is always somewhat dangerous because of the possibility of cardiac dilatation, more especially if there be a toxic state present. It is for that reason that many authorities recommend in pernicious anemia a small amount of blood, say 500 c.c., to be given repeatedly rather than take the risk of giving a larger quantity. Smaller amounts given every few days in severe anemias are often very efficacious. The excessive amount of blood is apt to do harm and to prevent bone marrow production.

For severe hemorrhages, one may give larger amounts because, under certain conditions, the blood platelets are diminished and must be restored. The diminution in the platelets may occur without any special diminution in the red blood-cells or with it. Platelets are said to have a life history of four days only, and for that reason the repetition of the transfusion under such conditions is imperative. In hemophilia, for example, a defect in platelets is the chief source of trouble, so that, with these, mild transfusions must be frequent and copious.[1]

The defects in platelets has suggested the advisability of bleeding the patient first, and then restoring the defect by normal blood in which the platelets are normal in quantity.

[1] In certain types of purpura (W. W. Duke) diminution of platelets is the important blood change.—Editor.

It may be taken as a general rule that transfusion is wise wherever coagulation time is delayed. It is for this reason that transfusion is specially useful before operation upon cases in which a hemorrhage may be anticipated, for example, patients with jaundice, for a transfusion supplies the extra quantity of platelets which might prevent an eventual hemorrhage.

Transfusion in Pernicious Anemia.—Transfusion is useful in relapses and to bring about remissions. It aids in keeping up the patient's general condition and gives the bone marrow a chance to act more normally. For this purpose, it may be used once every five to ten days. The results are shown quickly, even though not always of long duration. There is general well-being, the appetite improves, and fever, if present, diminishes.

Where, however, the patient shows excessive hemolytic activity, transfusion seems of little use. Such, at all events, was the experience of Minot and Lee. Their results cover a wide experience in a series of nearly 100 cases: out of 46 cases, 9 showed immediate marked benefit during various stages of the disease. Sometimes a first transfusion did not avail, and the second showed brilliant results. In other cases the improvement was either slow or moderate, and in 17 cases no good results followed. Ten patients died within a month after transfusion. These authors prefer using small amounts (500 c.c.) frequently instead of one copious transfusion.

Regarding the time to transfuse, the most favorable cases are those in which remissions seem to occur most frequently, and the time to select is that when improvement seems to be commencing. One should not transfuse at a blood crisis, nor when the patient is in a state of exacerbation, or very ill; early cases do better than those much advanced. One may watch for the regenerative power by estimating the red cell count, the hemoglobin, the white cells and the platelets. Cases which improve rapidly usually have shown marked stimulation, while those improving slowly show rising hemoglobin and cell counts, as well as increases in the number of platelets. The higher the polymorphonuclear count and the greater the number of platelets, the better is the regenerative power. It is the level of the hemoglobin rather than the red cells that coincides with well being.

Serum Therapy.—This differs from injections of defibrinated blood in that the serum separates only from the clot instead of the fibrin being whipped up and removed.

Horses that are repeatedly bled, for example, in the making of diphtheria serum, develop in their serum a kind of active hematopoietin, so that one may rationally give this serum to anemic patients, say in doses of 10 c.c., two or three times a week for two or three weeks, and manifest benefit may result, even greater than under arsenic and iron, and there need be no danger in the treatment.

The serum may sometimes be given in anemia with benefit by mouth in doses of 10 c.c. for four consecutive days, then rest twenty days and repeat again, always upon an empty stomach. Normal horse serum has also been given by mouth in dyspepsia, tuberculosis, etc., with good effect, which has raised the question whether the serum does not exert some stimulating effect on autocytolysis.

For the same reason such treatment might be used in cryptogenetic anemias of an unyielding character.

Gilbert and Weil record three successful cases treated with injections of 40 c.c. of blood-serum from a rabbit which had been repeatedly bled and rendered anemic. Great amelioration of the symptoms followed, but only of a temporary character, because the cause of the hemolysis evidently persisted.

Plasmotherapy.—Plasmotherapy has been much lauded, especially by the French, and several interesting theses have been written upon the subject. By plasmotherapy is meant the therapeutic use of the protoplasm of the cell freed from its envelope (hemoplase). The action is supposed to be based upon the chemical composition of the cell, upon a plasmic energy, and upon active principles, etc., acting according to the laws of immunity within its substance.

Plasmotherapy is considered by its supporters to be better than serotherapy, because antitoxic bodies are elaborated by the protoplasm and are only secondarily in the serum, and because it also contains the hemoglobin, lecithin, cholesterin, etc., present in the cell protoplasm. For a similar reason plasmotherapy should be better than opotherapy, because in opotherapy the protoplasm is inhibited by being shaken into extracts.

Thus hemoplase is a solution of blood plasma used in plasmotherapy. It is a solution, in an isotonic medium, of the active principles of blood corpuscles, the envelope of inert material being dissolved.

Method of Preparation.—The blood obtained by bleeding is at once mixed with a saline solution, energetically centrifugalized, and decanted. The corpuscles are washed with isotonic liquid several times and the original volume is restored with distilled water, then briskly frozen several times, heating each time to 35° C. This breaks the envelopes of the corpuscles and liberates the substance contained in the protoplasm. To separate the débris of cells centrifugalize again, decant the liquid, and make isotonic with saline solution, filter and preserve in sterilized flasks.

The blood from the sheep or ass will do, and thus prepared will keep from twelve to fifteen months. The resulting liquid is red, clear, and odorless, containing oxyhemoglobin. It must be kept below 30° C. to prevent coagulation. By weight 100 gm. is equivalent to 4.5 gm. hemoglobin. Toxicity is slight, it is non-irritant to the kidneys, and may be used subcutaneously.

Mode of Administration.—The usual mode is the administration of 10

to 20 c.c. intramuscularly every two or three days for ten to twelve doses.

Advantages.—Clinical experiments seem to show that it has antitoxic and tonic powers. Its absolute simplicity and innocuousness and the simple technic are features which commend it in place of transfusion or similar methods, and there is no danger of embolism. A more widespread use of this form of treatment is necessary before passing judgment upon its efficacy.

Piot, in his thesis, 1909, records eleven cures in several forms of anemia; none, however, pernicious in type.

Hemoplase may now be obtained commercially without the inconvenience of preparing it. It is made in the Lumière laboratory, Paris, by Dr. J. Chevrotier, and is sold in small sterile closed flasks, each containing 10 c.c., that is, the amount of one dose.

Hemolysin Treatment of Pernicious Anemia.—Courmont and André have recently investigated the therapeutic value of stimulation of the bone marrow by the inducing of mere destruction of blood. The observation of Bordet that the serum of animals injected with defibrinated blood becomes hemolytic led to the suggestion by Metchnikoff that such serum, if hemolytic in large doses, should stimulate hemopoiesis in small quantities. A series of experiments were done by Cantacuzène, Bielonsky, and Metchnikoff and Besredka on animals and human subjects, and on a series of patients suffering from mild grades of anemia, which verified Metchnikoff's hypothesis.

On the basis of these observations Courmont and André treated several cases of severe anemias by the injection of serum from two goats which had been rendered hemolytic by the injection of human defibrinated blood. The results warranted the following conclusions: (1) Injections of hemolytic sera produce an increase of red cells and an eosinophilia. (2) Such injections are painful and also the process is too complicated for general therapeutic practice. Moreover, slight anemias yield readily to treatment with iron. Therefore this measure should be reserved for use in the severe grades of anemia only that have shown themselves refractory to other means. (3) In the cases treated the results were favorable *in some,* while in others the condition remained intractable. Finally in all the remedial effect was temporary, not curative.

Engel, following a slightly different line of thought, treated a case of intractable chloranemia by repeated injections of rabbit serum which had been rendered hemolytic by the introduction of defibrinated blood from the anemic patient herself, the theory being that the toxin causing the anemia in her would give rise to its own specific antibodies. A cure resulted, no other line of treatment being employed.

While these investigations are of much interest the therapeutic value of the hemolysin treatment of anemia has not by any means been established.

Cholesterin.—The presence of cholesterin in the blood-cells was first made known by Hoppe-Seyler, and its presence in the serum was detected by Hurthle, and it has been demonstrated by successive observers in practically all the organs of the body, as well as in the bone marrow, subcutaneous fat and milk. In the red blood-cells it exists in proportions of 0.04 to 0.06 per cent. In the serum, 0.234 to 0.19 per cent.

Its physiological importance, however, was not recognized until very recently, when the studies of the lipoid bodies, of which cholesterin is one, have shown the marked antihemolytic powers which cholesterin possesses both in vitro and in vivo.

Reicher showed that the hemolysis of kobralezithid can be checked by giving cholesterin to rabbits. A proof of the increased accumulation of cholesterin in the blood-serum is furnished by the fact that serum of animals immunized in this way by cholesterin furnishes a much higher protection against saponin hemolysis than the serum of untreated control animals. Further, the well-developed anemia produced in animals by kobralezithid can be almost completely banished by cholesterin treatment, and urobilin disappears from the urine, showing that the hemolysis has been checked.

It is reasonable to suppose, therefore, that cholesterin given to anemic individuals should, on the same principle, produce a rise of cholesterin in the blood and create protection against hemolysis. As cholesterin esters are not antihemolytic the greater part of the increased cholesterin must exist free in the blood.

Klemperer is among those who regard its use with favor. He explains the usefulness of the drug as the exertion of an inhibitory action upon an antikatalytic substance, rather than by assuming any direct combination between it and the poison of anemia. He remarks that while the antihemolytic powers of cholesterin have been proved in vitro, and also in experimental animals, it is not at all clear that in pernicious anemia the virus at work is hemolytic in character.

He points out that while cholesterin in oily solution is very unpleasant to take, the treatment may be carried out in the food without artificial medication, by giving much milk, cream, and butter as above. Eight cases of pernicious anemia were thus treated by him with marked benefit. In only one of these, however, was the patient treated by this method alone and without arsenic. He concludes both from his own results and from those of Reicher that while cholesterin checks to some extent the action of the poison of pernicious anemia it does not exert any decisive effect upon its course.

Iscovesco likewise found it useful in certain hemorrhagic conditions, purpura, as well as in chlorosis and lymphadenoma, though not in pernicious anemia. To him it seemed also that the cholesterin protects the human blood-cells against serums and other hemolytic substances. (For

the investigations of Pringsheim and others on cholesterin in paroxysmal hemoglobinuria see Chapter XXXVIII, page 899, Hemorrhagic Diseases.

Other investigations, however, seem to show that cholesterin has practically no action on the globular resistance of the rabbit, even though injected in a 3 per cent oily solution which neutralizes hemolysin in vitro.

Dose.—From 30 to 45 gr. (2.00 to 3.00 gm.) are used daily, dissolved in 100 c.c. of olive oil, making a 3 per cent solution. This may be taken in capsules, 15 c.c. in each, or it may be flavored with Ol. menth. pip. and taken in teaspoonful doses throughout the day. Or 33 gr. (2.10 gm.) may be given daily in one liter of cream and 200 gm. of butter, for these substances contain cholesterin esters to the required amount.

Organotherapy.—In pernicious anemia this is expressed in the use of bone marrow. It is doubtful if bone marrow in pernicious anemia is useful for anything else than as a mere food. According to some its main benefit arises from the glycerin with which it is prepared, for, as we shall see later, glycerin in itself is recommended as efficacious in the treatment of severe anemia. We are indebted to the French for their advocacy of bone marrow therapy, and they recommended it especially in those cases where myelocytes and normoblasts swarm, that is, where great activity of the bone marrow is obvious. On the other hand, they regard it as useless in the aplastic variety.

One usually selects the raw marrow from the long bones of the calf, and gives at least 2 to 3 ounces daily. It may be used in the form of sandwiches, as recommended by Fraser, or in well-seasoned broth—or a glycerin extract may be made with alcohol, though no preparation is so good as the fresh marrow bone.

The following prescription is sometimes used in the form of a jelly:

Red marrow, 1 part.
Port wine, 3 parts.
Gelatin, q. s.
Glycerin, q. s.

Hurter prescribes bone marrow in support of other measures in the form of tablets, as follows:

Marrow	90 parts
Port wine	30 parts
Glycerin	30 parts
Gelatin	20 parts

Mix the marrow and wine in one hot mortar, the glycerin and gelatin in another, and then combine and form in tablets. They will keep for months.

Cech reports a case of pernicious anemia treated with 0.50 gm. fresh calves' marrow daily for five weeks, with marked remissions for a time, but later on a fatal result. In this case no myeloid reaction was visible.

Pancreatin.—On the theory that the same principles hold good in the organism in relation to immunity as to protective ferment, and arguing from the facts that diphtheria antitoxin contains an increasing amount of antitrypsin with increasing immunizing power, and that an unusually high antiferment content of the blood is an important feature of exhausting diseases, Brieger proposes the possibility of restoring normal relations in pernicious anemia by the administration of pancreatin. He treated three cases by combining this with arsenic, giving the pancreatin before and liquor arsenicalis after meals. Rapid improvement followed with a rapid drop in the antitrypsin content of the blood. The results were not permanent, however, two of the patients having died since of the disease. The third has been under observation three years.

Glycerin.—Vetlesen reports remarkable results in two cases from the use of glycerin. One tablespoonful was given three times a day with the juice of half a lemon.

In one case after one month's treatment the red cells rose from 990,000 to 4,360,000, and the hemoglobin from 20 per cent to 69 per cent. He thinks the success of the organic extracts of the bone marrow depends upon the glycerin with which these are extracted.

Tallquist and Faust believe that pernicious anemia is a result of poisoning by oleic acid, and that glycerin combines with this to form a harmless compound.

The Antiseptic Treatment of Pernicious Anemia.—But little can be said as to the very great benefit that has been ascribed to the use of antiseptics. It was supposed that these might act against the infective processes which produce hemolysis.

William Hunter recommended oral asepsis with forced feeding and serum therapy, but the results of his treatment, except in the case of ordinary secondary anemias, are more than doubtful.

Many so-called intestinal antiseptics have been recommended, and various degrees of improvement have been recorded. It must always be remembered that remissions frequently occur spontaneously, and many writers believe in the efficacy of no treatment whatever, or do not believe in the efficacy of any treatment whatsoever, so that even when occasional improvement is recorded by the use of glycerin, carbolic acid, bichlorid of mercury, beta-naphthol, bismuth or salol, the relations between cause and effect must be first proven.

In the same category come such treatments as gastric lavage and intestinal irrigation. Apart from their aid in the administration of arsenic their value is very dubious.

Strümpell, indeed, regards lavage as quite useless. But this is not the

only extreme tried in the treatment of pernicious anemia. Burch has even recommended appendicostomy and intestinal lavage through the opening, while others have recommended the use of antistreptococcic serum, because, forsooth, streptococci were found in the mouth and teeth. Certainly if this serum is of any benefit it is quite apart from its specific action upon streptococci.

The Treatment of Special Symptoms.—The gastro-intestinal symptoms require special care. Apart from watching the arsenic and the diet it will be found necessary to keep such patients at rest, and where *diarrhea* exists to give bismuth salicylate.

Where *constipation* exists, on the other hand, great care should be exercised regarding purgatives and only the mildest laxatives should be given.

Where *hemorrhages* occur the treatment should be as much as possible local or combined with transfusion. Nasal or uterine bleedings should be treated by adrenalin chlorid on gauze tape. For *intestinal hemorrhages* food should be withdrawn and styptic pill administered with lead and opium. Where the bleeding is low down in the bowel astringent lavage may be helpful. For hematemesis ice, silver nitrate, and withdrawal of food are usually all that is necessary. *Bad teeth* should always be treated, tartar removed, and useless stumps extracted, cavities cleaned and stopped. *Pyorrhea alveolaris* should be treated with the brush and some such wash as hydrogen peroxid.

Insomnia is not uncommon, but where it is present a gentle hypnotic is usually sufficient.

Where *cord pains* occur it is well to bandage the legs, which must be kept at rest, and if necessary sedatives may be administered.

REFERENCES

Naegeli, Otto. Blutkrankheiten und Blut Diagnostik, Leipzig, Verlag von Veit und Comp., 1908.

Pappenheim. Prologomena zum Capitel Anemie, Folia hæmatol., ix, ii, 3, 4, 1910.

Chlorosis and Secondary Anemias

General Articles

Allbutt, Sir C. Chlorosis, Allbutt and Rolleston's System of Medicine, v, 681-725, 1909.

Cabot, Richard C. Article on Chlorosis in Osler's Modern Medicine, iv, 639, 1908.

Ferreira. Treatment of Chlorosis, Presse méd., Nov. 7, 1908.
Huchard and Fiessinger. Le Traitement des Anémies, Journ. des Praticiens, 41, 42, 1908.
Virchow. Uber die Chlorosen u. Anomalien in Gefäss-apparate, Berlin, 1872.
Von Noorden. Die Bleichsucht, Nothnagel's Spec. Path. u. Therap., 1897; viii, ii, edited by Stengel, English ed., 1905.

Hydrotherapy

Armbrust. Hydrotherapy in Anemia and Chlorosis, Journ. de physiothérap., July 15, 1909.
Ferrario. On the Treatment of Chlorosis, Gazz. degli Ospid., Aug. 12, 1909, Synop., Arch. mal. du cœur, Dec. 19, 1910.
Wandel. Beitrag zum Wesen und Therapie der Chlorosen, Deutsches Arch. f. klin. Med., xc, 52, 1907.

Action of Iron

Arneth, Joseph. Diagnose und Thérapie der Anämien, A. Stuber, 140-164, Wurzburg, 1907.
Evans. Brit. Journ. Exper. Path., ii, 105, 1921.
Maillart. Cor.-Bl. f. schweiz. Aerzte, June, 1916.
Mayer, Erich. On Absorption and Elimination of Iron, Ergebn., d. Physiol., v, 1906.
Musser. Arch. Int. Med., xxviii, 631, 1921.
Stockman. Treatment of Chlorosis by Iron and Some Other Drugs, Brit. Med. Journ., i, 881, 942, 1893.
——— Summary of Sixty-three Cases of Chlorosis, Edin. Med. Journ., xli, 413, 1895.
——— Observations on the Causes and Treatment of Chlorosis, Brit. Med. Journ., ii, 1473, 1895.
——— Analysis of Iron in the Liver and Spleen in Various Diseases Affecting the Blood, Brit. Med. Journ., i, 1077, 1896.

Organic Iron

Clemm. Uber ein neues Blut Präparat (Hämoptan), Berl. klin. Wchnschr., 33, 1907.
Hauschild. Uber Euferrol, Deutsche med. Wchnschr., 26, 1907.
Kraus. Uber Triferrin, Therap. Monatsh., Oct., 1903.
Matzer. Klinische Untersuchungen ueber die Eisensomatose, Die Heilkunde, 1903, Synop., Folia hæmatol., i, 1904.
Oerum. Organic and Inorganic Iron Preparations (Hematin Albumin), Ztschr. f. exper. Path. u. Therap., iii, 1, 145, 1906.

Hypodermic Use of Iron

Glaevecke. Uber subcutane Eiseninjectionen, Arch. f. exper. Path. u. Pharmakol., 1883.

Morse. Treatment of Anemia in Infancy by Subcutaneous Administration of Citrate of Iron, Journ. Am. Med. Ass., July 10, 1909.

Arsenic and Iron Compounds

Aubertin. Presse méd., May, 1914.

Provinziali. New Preparations for the Cure of Anemia (Metarsyl and Iron Metarsyl), Gli. Incurabile, 1908, 1; Synop., Folia hæmatol., April, 1910.

Salkowski. On a New Ferric Compound Containing Also Phosphorus and Arsenic, Berl. klin. Wchnschr., 4, 1908.

Manganese

Viccinimi. On the Hematogenous Capacity of Manganese, Synop., Folia hæmatol., 1, 1907.

Cholesterin

Iscovesco and Fronty. Pernicious Anemia.

Serum Therapy

Delearde and Paquet. Serum Therapy of Chlorosis and Certain Symptomatic Anemias, Echo méd. du nord, May 2, 1909, Long Synopsis Arch. mal. du cœur, Dec., 1909.

Gartolari. Antibodies in the Treatment of Chloranemias, XVième Cong. Ital. de Méd., Gênes, 1909; Synop., Arch. mal. du cœur, 604, 1908.

Hort. Therapeutic Uses of Normal Serum, Lancet, Feb. 15, 1908.

Tixier. Reactions of Bone Marrow in Gastroenteritis of Infants Treated by Physiological Serum and Seawater, Compt. rend. Soc. de biol., 394, 1908.

PERNICIOUS ANEMIA

General Articles

Addison. On the Constitutional and Local Effects of Disease of the Suprarenal Capsules, 1855, Republished in Addison's Complete Works, New Sydenham Soc., 211, 1868.

Biermer. Form von progressiver perniciöser Anemie, Cor.-Bl. f. schweiz. Aerzte, ii, 15, 1872.

French, Herbert. Pernicious Anemia, Allbutt and Rolleston's System of Medicine, v, 727 to 757, 1909.
Hunter, W. Is Pernicious Anemia a Special Disease? Practitioner, xli, 81, 1888.
——— The Specific Infective Nature of Addison's Anemia, Brit. Med. Journ., ii. 1299, 1907.
——— Severest Anemias, i, 1909.
Quincke. Uber perniciöse Anemie, Volkmann's Sammlung, 100, 1876.
——— Weitere Beobachtungen ueber perniciöse Anemie, Deutsches Arch. f. klin. Med., xx, 1, 1877.

Hydrochloric Acid

Carr. Am. Journ. Med. Sc., v, 160, p. 737, 1920.
Croftan. Note on the Treatment of Pernicious Anemia, Journ. Am. Med. Ass., Aug. 13, 1910.
——— Die Salzaurebehandlung der perniciosen Anemie, Deutsche med. Wchnschr., Dec. 19, 1912.
Hess. Reichs-Medizinal-Anzerger, No. 22, 674, 1911.

Arsenic

Bloch. Action de l'Arsenic sur le Sang et les Organes Hemopoietiques, Thèse de Paris, 1908.
Bramwell, Byrom. Arsenical Treatment of Pernicious Anemia, Clinical Studies, 1902, 1906, 1909.
——— Brit. Med. Journ., i, 209, 1909.
Fowler. Medical Reports on the Internal Use of Arsenic in the Cure of Agues, Remittent Fevers, etc., London, 1786.
Gunn. Action of Arsenic on the Red Corpuscles and Theory of the Blood Defect in Pernicious Anemia, Brit. Med. Journ., July 18, 1908.
Gunn and Feltham. On the Hemolytic Action of Arsenic, Brit. Med. Journ., Jan. 21, 1911.
Fefèvre. Les Arsenicaux en Thérapeutique, Thèse de Paris, 1907.
Vaugeon. Le Cacodylate de Fer dans les Anémies, Thèse de Paris, 1902.

Atoxyl

Heinrich. Einige Bemerkenswerthe Fälle von Arsazetin Behandlung mit historischen und kritischen Bemerkungen, Therap. Monatsh., 593, Nov., 1910.
Klemperer. Zur Behandlung der perniciöser Anemie, Berl. klin. Wchnschr., No. 52, 1908.

Kuhn and Aldenhowen. The Importance of a Lessened Oxygenation of the Tissues in the Stimulation of Blood Formation, with Experiments on the Secondary Action of Medicaments (Atoxyl and Tuberculin) on New Blood Formation, Synop., Folia hæmatol., April, 1910.
Naegeli. Uber die Behandlung pseudoleukemischen Affectionen mit Arsazetin, Therap. Monatsh., Feb., 1910.
Neisser. Deutsche med. Wchnschr., 35, 1908.
Reicher, K. Etiologische und therapeutische Versuche bei perniciöser Anemie, Berl. klin. Wchnschr., Oct. 12 and 19, 1908.
Senator. Therapeut. Rundschau, 9, 1909.

Salvarsan

Boggs. Johns Hopkins Hosp. Bull., Oct., 1913.
Bramwell, Byrom. Salvarsan in Pernicious Anæmia, Brit. Med. Journ., 1911; June 22, 1912.
Evans. Arch. Int. Med., xvii, 1916.
Hobhouse. Salvarsan in Pernicious Anæmia, Brit. Med. Journ., Dec. 14, 1912.
Leede. München. med. Wchnschr., lviii, 1184, 1911.
Maynard. Salvarsan in Pernicious Anæmia, Brit. Med. Journ., Jan. 11, 1913.

Splenectomy in Pernicious Anemia

Bruhn-Fabrous. Quoted in N. Y. Med. Journ., March, 1916.
Decastello. Deutsche med. Wchnschr., xl, 1914.
Eppinger. Zur Pathologie der Milzfunctionen, Berl. klin. Wchnschr., Nos. 33, 34, Aug. 18, 25, 1915.
Giffin. Minn. Med., 831, March, 1921.
Giffin and Szlapka. Journ. Am. Med. Ass., lxxvi, 290, 1921.
Giffin, Szlapka, Minot and Lee. Bost. Med. & Surg. Journ., 831, Nov. 17, 1921.
Huber. Berl. klin. Wchnschr., xlvii, 1913.
Jagic. Wien. klin. Wchnschr., xxvii, 1913.
Klemperer and Hirschfeld. Splenectomy in Pernicious Anæmia, Therap. d. Gegenwart, No. 54, 1913.
——— Journ. Am. Med. Ass., Sept. and Oct., 1913.
Krumbhaar. Proc. Am. Med. Ass., 1916.
Lee, Vincent, and Robertson. Journ. Am. Med. Ass., 1915.
Mosse. Berl. klin. Wchnschr., xlvii, 1913.
Port. Ibid., li, 546-548, 1914.
Roblee. Journ. Am. Med. Ass., lxiv, 1915.

Transfusion

Bernheim. Therapeutic Possibilities of Transfusion, Journ. Am. Med. Ass., July 26, 1913.

Bovaird, David. Transfusion of Blood in Three Cases of Pernicious Anemia, Med. Rec., Feb. 11, 1911.

Cahn. Transfusion of Blood in Pernicious Anæmia, Synop., Folia hæmatol., 264, April, 1910.

Huber. Treatment of Severest Anemias with Blood Injections, Deutsche med. Wchnschr., June 9, 1910.

Morawitz. Die Behandlung schwerer Anämien mit Blut-transfusionen, München. med. Wchnschr., 767, 1907.

Ottenberg and Libman. Am. Journ. Med. Sc., 1915.

Rehling and Weil. The Avoidance of Hemolysis in Transfusion, Am. Journ. Surg., March, 1909.

Satterlee and Hooker. Journ. Am. Med. Ass., Feb. 26, 1916.

Vogel and McCurdy. Arch. Int. Med., Dec. 15, 1913.

Weber. Transfusion of Blood in Treatment of Anemia, Monthly Cyclo. and Med. Bull., Dec., 1910.

——— Uber die Behandlung schwerer Anämien mit Blut-transfusionen, Deutsches Arch. f. klin. Med., xcvii, 165, 1909.

——— Uber intravenose Injektionen Kleiner Mengen von Menschenblut bei der Behandlung schwerer Anämien, München. med. Wchnschr., June 17, 1913.

Serum Therapy

Gilbert and Weil. Clinical Study of Three Cases of Pernicious Anemia, Arch. mal. du cœur, 553, 1908.

Plasmotherapy

Chaveau and Lumières. Acad. d. Sc., Paris, 1905.

Gelibert. Plasmotherapy in Tuberculosis, Internat. Congress of Tuberculosis, Paris, 1905.

Piot. La méthode plasmothérapique et la Plasmothérapie sanguine, Thèse de Lyon, 1908.

Santini. L'Application de l'Hemoplase Lumière à la Sérothérapie, L'Avenir Médicale, 1911.

Opotherapy

Cech. Medullary Opotherapy in Pernicious Anemia, Synop., Folia hæmatol., April, 1910.

Hurter. Med. Klin., Dec. 31, 1912. Quoted by Stengel, Progressive Medicine, June 1, 1913.

Hemolysins

André. Injections de Sérum Hémolytique aux Anémiques, Thèse de Lyon, 1903.

Bielonovsky. De l'Action des Differentes Doses de Sérum hemolytique sur les elements du Sang, Thèse de Saint Petersburg, 1902.

Bordet. Les Sérums Hemolytiques, Leurs Antitoxins et les Theories des Sérums Hemolytiques, Ann. de l'Inst. Pasteur, 1900.

Cantacuzène. Sur les Variations Quantitatives et Qualitatives des Globules Rouges Provoquées chez le Lapin par les Injections de Sérum Hémolytique, Ibid., June, 1900.

Courmont and André. Injections des Sérums Hémolytiques à des Malades Anémiques, Journ. de phys. et path. gen., Jan., 1904.

——— Utilization Thérapeutique des Sérums Hémolytiques, Folia hæmatol., 389, 1904.

——— Sur les Cytotoxins, Ann. de l'Inst. Pasteur, June, 1900.

Metchnikoff et Besredka. Action de l'Hémotoxin sur l'Homme, Ibid., June, 1900.

Antibodies

Engel. Uber einen versuch, mit Hülfe des Blutserums eines Anemischen, einen therapeutisch verwendbaren specifischen Antikörper herzustellen, Ztschr. f. klin. Med., liv, 154, 1904.

Norso, Perouse. Treatment of Anemia by Antibodies, Synop., Folia hæmatol., i, 1907.

Cholesterin

Fronty. La Cholésterine et son Rôle Antihémolytique, Thèse de Paris, 1909.

Iscovesco. Presse méd., July 18, Aug. 19, 21, 1908.

Klemperer. Loc. cit., Atoxyl.

Morgenroth and Reicher. Anemia Caused by the Toxolecithid of Cobra, Berl. klin. Wchnschr., 1200, 1907.

Pribram. La Cholestérine, Biochem. Zeitschr., i, 1906.

Reicher. Loc. cit., under Atoxyl.

Tallquist. Pathogenesis of Bothriocephalus Pernicious Anemia, Ztschr. f. klin. Med., lxi, 1907.

Glycerin

Vetlesen. Casuistic Contribution to the Latest Investigations into Pernicious Anemia, Norsk. Mag. f. Laegvidensk., 1152, 1908.
——— 1909, 1041, Synop., Folia hæmatol., April, 1910.
——— Value of Glycerin in Pernicious Anemia, Med. Rev., London, xii, 157, 1909.

Intestinal Antisepsis

Burch. Appendicostomy in Pernicious Anemia, Journ. Am. Med. Ass., March 13, 1909.
Butsch and Ashby. Factors in Reactions after Blood Transfusions, N. Y. Med. Journ., cxiii, 1921.
Culpepper and Ableson. Journ. Lab. & Clin. Med., vi, 276, 1921.
Dill. Pernicious Anemia Treated by Lactobacillin, Proc. Roy. Soc. Med., Clinical Section, ii, 21, 1909.
Grawitz, E. Neuere Erfahrungen über die Therapie der perniciösen Anemien, Deutsche med. Wchnschr., 1092, 1135, 1904.
Hoffmann and Habein. Journ. Am. Med. Ass., 76, 1921.
Levine and Segall. Surg., Gynec. & Obst., Sept., 1922.
McClure and Dunn. Transfusion of Blood, Johns Hopkins Hosp. Bull., xxviii, 99, 1917.
Meleney, Stearns, Fortuine and Ferrey. Am. Journ. Med. Sc., civ, 733, 1917.
Miller, G. N. Y. Med. Journ., April, 1921.
Ravdin and Glenn. Transfusion of Blood, with Report of 186 Transfusions, Am. Journ. Med. Sc., clxi, 705, 1921.
Robertson and Rous. Sources of the Antibodies Developing after Repeated Transfusions, Journ. Exper. Med., xxxv, 141, 1922.
Sellards and Minot. Journ. Med. Research, xxix, 469, 1916.
Unger, L. Journ. Am. Med. Ass., Jan., 1921.
Vogel. Journ. Am. Med. Ass., 1916.

Pancreatin

Brieger. Pancreatin in Pernicious Anæmia, Deutsche med. Wchnschr., No. 46, Nov. 14, 1912.

Radium, Thorium-X, Actinium-X

Arneth. Berl. klin. Wchnschr., Jan. 26, 1914.
Bickel. Thorium-X in Anæmia, Leukemia and Rheumatism, Berl. klin. Wchnschr., Feb. 24, 1913.

Brill and Zehner. On the Action of Soluble Radium Salts on the Blood Picture, Strahlentherapie, Berl. u. Wien, i, 347-357, 1912.

Jona. Journ, Am. Med. Ass., 66, 1916.

Lazarus. Actinium-X Treatment, Especially on Pernicious Anæmia, Berl. klin. Wchnschr., Nov. 25, 1912.

Park. Thorium-X in Treatment of Pernicious Anæmia, Med. Rec., Mar. 8, 1913.

Plesh. Uber die Dauer der therapeutischen Wirkung des Thoriums, Berl. klin. Wchnschr., 2305, 1912.

CHAPTER XXXVI

LEUKEMIA AND HODGKIN'S DISEASE

C. F. Martin

LEUKEMIA

This disease of the blood-forming organs, which was first described by Virchow and Hughes Bennett in 1845, and later by Neumann and Ehrlich, is yet even far from being thoroughly understood. Its characteristic features are hyperplasia of the leukoblastic tissues and more or less increase in the leukocytes of the peripheral circulation.

Originally two forms were described by Virchow—the splenic and lymphatic varieties, until Neumann demonstrated a probable origin in the bone marrow. This gave rise to the conception of a third variety; but Ehrlich, in his epoch-making work on this subject, showed that two great varieties alone existed, the one lymphatic, originating in the lymphatic tissues throughout the body (*lymphoplastic*), the other myelogenous (*myeloplastic*), taking its origin, at all events chiefly, in the bone marrow. While it is not even yet determined to what extent these two forms are correlated or interdependent, yet, for clinical purposes, this classification will serve as a basis of therapeutics in this article. It is important, however, to realize that all forms of leukemia must be regarded, not as maladies of local origin, but as system diseases in which the hematopoietic apparatus in general undergoes selective hyperplasia.

Pappenheim defines them as autonomous, but cryptogenetic, primary malignant constitutional hyperplasias elective of the hematopoietic cytoblastic tissue parenchyma.

The new tissue is, however, not mere overgrowth of preformed cells, for heterotopia and metaplasia occur. Lymphocytes and myelocytes are found in places in which they do not normally occur postembryonically, for example, myeloid metaplasia of the spleen occurs in myelogenous leukemia, and also lymphadenoid microlymphocytic metaplasia of the bone marrow in the lymphatic type. Metastases, if they occur, are of minor importance. New cells are morphologically and chemically normal cells,

thus differing from lymphosarcoma, and, although transitional and embryonic forms appear, they also adhere to the type of the immature blood cell.

The leukemias are leukemic forms (with special blood symptoms) of the aleukemic process known as pseudoleukemia; and, vice versa, pseudoleukemia is merely an aleukemic leukemia, both conditions being characterized by hyperplasia of the hemopoietic apparatus.

Both lymphatic and myelogenous forms of leukemia may be acute or chronic, and it may be said in general that all transitions occur, not only between these two forms histologically, but also clinically. Atypical forms likewise occur, such as chloroma, leukanemia, etc. It is important, however, where possible, to make a differential diagnosis, because the prognosis and therapeutics differ accordingly. The cause is undetermined, though some authorities are convinced that a toxin of exogenous or autointoxicative origin is at work.

Lymphatic Leukemia

The Chronic Type.—In this condition there is chronic hyperplasia with increased function of the lymphoid tissues throughout the body. The lymph glands are especially swollen; multiple lymphoid cell aggregations occur in all tissues and organs; the spleen is moderately enlarged; while, in the bone marrow, lymphoid elements are more or less predominant features. The thymus gland, the tonsils, the liver, the intestines, etc., all show multiple lymphomata.

The etiology of the disease is unknown. Its duration is, on the average, from three to five years, though cases have been recorded which have lasted more than thirteen years.

The Clinical Picture.—Patients afflicted with this disease usually show progressive weakness or emaciation, with pallor and gradually increasing painless enlargement of the lymphatic glands throughout the body. The cervical glands are usually first affected. Acute inflammatory disturbances are rare, though one may have fever, hemorrhage and local inflammations (tonsils). With development of the disease the liver and spleen increase somewhat in size, the bones are tender, but the metabolism is practically unchanged.

The blood, however, shows characteristic features; the small lymphocytes predominate, often forming 90 per cent of the leukocytes, and sometimes the large lymphocytes are increased. Myelocytes, on the other hand, are uncommon, but when present are of the fully matured variety. Leukocytosis is the rule, but a few cases with a leukopenia, but relative lymphocytosis, are recorded. The red cells and hemoglobin may be unchanged, though, with the development of the disease, there is diminution of both. Likewise, as the disease progresses, there are poikilocytosis,

polychromasia, and cells with basophilic granulations, and usually some nucleated red blood-cells and a few megalocytes.

The treatment is for the most part similar to that of the chronic myeloid form, the only difference being in the symptomatic considerations, where and when they arise.

The Acute Type.—The acute lymphatic leukemia is but a variety of the *chronic,* and is often hard to differentiate from it. The disease develops quickly, with fever, hemorrhages, gangrene of the mucous membranes, rapid anemia, and profound prostration; and, in the course of a few days, weeks, or months, death ensues.

Histologically the picture resembles that of the chronic variety. There is, however, a greater anemia, as a rule; there are often more of the large lymphocytes, but atypical blood-pictures are common.

Myelogenous Leukemia

In this form there is extensive hyperplasia of the myeloid tissue of the bone marrow, and myeloid metaplasia in the other tissues of the hemopoietic system. Not only, then, does the bone marrow show this change, but in the spleen, the liver, the lymphatic glands, and tissues there is very marked predominance of granulocytes and myeloblasts.

Here, too, the etiology is unknown, the disease is fairly uncommon and the duration averages several years.

The Clinical Picture.—As a rule, the disease is ushered in with signs of general malaise, and patients show weakness, pallor, some emaciation, and disturbance of digestion. The spleen enlarges early, and is often the only cause for which patients seek medical aid. Gradual dyspnea, cough, fever, sweating, and palpitation ensue, and, later on, hemorrhages from the skin or mucous membranes; defective vision and hearing are not uncommon. Enlargement of the glands usually follows soon after the splenic tumor has formed, though sometimes this feature may be quite absent. Infiltrations of the skin are not uncommon. With advancement of the disease there are pressure signs from enlarging glands in the thorax and elsewhere. The blood is pale, almost sticky, and very soon after the onset of the disease there is marked diminution in the red cells and hemoglobin, with increase in the blood platelets. The red cells show the usual changes occurring in grave anemias, and the white cells are enormously increased. Myelocytes predominate. While the polymorphonuclear leukocytes may be relatively normal in amount, there is always an increase in all forms of myelocytes (neutrophil, eosinophil, and mast). In other words, the granular cells are notably increased, while the nongranular elements, though also increased in numbers, are least of all affected.

The myelocytes in this form of leukemia show all transition forms,

thus differing from those seen in lymphatic leukemia, where the myelocytes are mature. Nucleated red cells are common, and there is nearly always a marked anemia. Aleukemic intervals may occur, and these often follow treatment. The interval is, as a rule, short-lived.

General Treatment.—There is no specific for any form of leukemia, nor is there any cure. In the present state of our knowledge the most that can be hoped for is the relief of symptoms and the prolongation of life. The course of the disease, as has already been said, is very variable, the acute cases terminating in a few days or weeks, and the chronic cases sometimes lasting for many years. In quite a few cases there seems to be a spontaneous improvement regardless of any form of treatment.

The prognosis would seem to be more grave in youth, also where a great anemia exists, or where there are hemorrhages into the skin or from the mucous membranes. The presence of diarrhea or dropsy likewise adds to the gravity of the prognosis, and renders treatment all the more hopeless. There is probably not much relation between the immediate prognosis and the condition of the blood. According to some authorities, in the mixed forms of leukemia in which lymphocytes and myelocytes together predominate in the blood, the prognosis is more unfavorable. And others, again, say that the form of leukocytosis is not necessarily of any prognostic value. Where cachexia develops from intercurrent infections, the prognosis is grave and the end probably near.

Rest in bed is imperative, and the patients, in consequence, should avoid exertion of any kind, mental or physical; all excesses should be avoided, the diet should be nourishing and non-irritating; no drastic purgatives should be given. The modern treatment demands the use of three methods:

1. The use of radio-active elements, X-rays and radium, of which the latter is undoubtedly the more efficacious.
2. The use of benzol.
3. Arsenical treatment.

Radiotherapy—*Historical Note.*—The treatment of leukemia by X-rays emanated in the first place from America, where the first application was made by Pusey in 1902. In the following year Senn reported two cases, one of leukemia and one of pseudoleukemia, with marked improvement. Skepticism was at first shown in Germany, until Krone and Ahrens published successful cases in 1904. Full studies of the histological appearances and changes in metabolism were made by Krause, Heinecke and Ziegler. A wealth of literature followed.

That the X-rays form a valuable adjunct to therapeutics is now beyond any doubt, and that they have a beneficial effect that is sometimes permanent in the treatment of diseases of the external tissues and superficial glands is likewise everywhere recognized. The experience of Des-

plats, who caused a mass of cervical glands to disappear under this treatment, is now a very common event, and the disappearance in many cases seems permanent. It is less common, perhaps, to find the deeper glands disappearing under this treatment, though Elischer and Engel cured two massive mediastinal tumors by radiotherapy; in each case scar tissue of small size remained, and the subjective and objective symptoms were entirely relieved.

Dupeyral, discussing the effect on adenitis, notes that on normal glands the X-rays have no effect, that they rapidly cure most inflammatory conditions of the glands, and that they have a most remarkable effect on the hard fibroid tuberculous variety. Where these glands suppurate, they should be incised and the pus should be removed and the X-rays then applied.

The value of radiotherapy in leukemia has been the subject of much research and discussion, the action being ascribed to various causes. The results on the whole are regarded as palliative, as delaying the fatal issue, and as being at present the most satisfactory mode of treatment at our disposal.

Mode of Action of Roentgen Irradiation.—Several theories find acceptance. Of these only two need mention. *The cellular theory,* supported by Grawitz, Barmon and Linser, Mosse, Ziegler, Krause, Tatarskey and Wolby, and others, is based on the changes in lymphoid tissue taking place after irradiation, such as rarefying of cellular structure, hypoplasia of follicles, etc. The X-rays are claimed to have a definite specific action on lymphoid tissue everywhere, the bone marrow being affected last. This theory is probably, at least in part, true. Heinecke established the selective action of X-rays on bone marrow and lymphoid tissue, and Warthin, in a most interesting series of observations, confirmed this work. Certainly lymphoid, myeloid, and epithelioid cells are most affected by Roentgen rays, with resulting degeneration and disintegration.

Upon normal individuals Demieville found that irradiation reduces the number of white blood-cells by 400 to 1,000 per cm.

The effect is complex, depending on various conditions, namely, the dose, the region and surface irradiated, the individual susceptibility, and the state of the individual's hemopoietic organs, especially his lymph glands. One irradiation of half an erythema dose on an indifferent region causes leukopenia and cell destruction. Repeated and fractional doses cause hyperleukocytosis, according to area treated, and later young forms appear, some of which are abnormal degenerated cells, while later still myeloid reaction occurs, especially when myeloid tissue is irradiated, and this reaction seems to lessen with each subsequent treatment. Eosinophils reach their minimum in four days. Red blood-cells vary little, at first increasing slightly and then diminishing in number. The hemoglobin slowly lessens in percentage. Cells become degenerated in the cir-

culation, but Warthin's researches on tissues irradiated show that leukocytes degenerate even till their number is subnormal (aleukia) and then a limit is reached or an adaptation attained, with changes in the hemolymph glands and bone marrow. A lower type of leukoblastic tissue is developed with more primitive but more resistant cells. He concludes that the action of X-rays is degenerative and inhibitory but not curative, the essential leukemic process not being thereby arrested.

Krause and Ziegler demonstrated the predilection for young cells, and proved that X-rays killed the experimental animals by complete destruction of the cells in the blood-forming organs and leukocytes in the blood, while inducing in the early stages degeneration in the spleen, temporary polymorphonuclear hyperleukocytosis, and then a disappearance of leukocytes. Under gentle irradiation the spleen showed early destruction of lymphoid tissue, while hyperfunction occurred in the bone marrow, a secondary myeloid change. They upheld Ehrlich's dual theory that the antagonism of the myeloid and lymphoid series of cells is kept in equilibrium by spleen and bone marrow.

It is now generally recognized that Roentgen irradiation has a selective action for lymphocytes and myelocytes—hence its use in leukemia. Improvement occurs because these cells are removed from the blood and tissues where they collect. This, however, is a palliative, not a curative, measure.

Oettinger, *et al.,* observed the cellular effects in leukemia treated by X-rays with the following results:

In *myeloid* leukemia, splenic irradiation caused, first, slight polynuclear increase, and then rapid diminution of white cells, according to the amount of X-rays absorbed. Myelocytes and eosinophils diminished in number, though the percentage of the polynuclears was increased. Red cells also increased. The spleen diminished rapidly. Strength and appetite improved, but, after a time, relapses occurred, nor could the fatal result be averted.

In *lymphatic* leukemia, lymphocytes diminished under treatment and the polynuclear percentage was increased. The white cells as a whole became less. The spleen and glands lessened in size and showed macrophage phenomena. It does not seem that there is an elective destruction in the circulating blood of the lymphocytes. On the contrary the difference in effect on the two systems of hemopoietic organs seems to come from filtration of rays through to the bones.

The radiosensibility of various types of cells has been studied with illuminating results by different observers.

Henri Béclère and Bulliard studied the effects on various forms of leukocytes, and their results may be epitomized by examination of the subjoined tables showing the effects before and after treatment.

M. B. 39 Years Old. Before Treatment, Aug. 28, 1908. Leukocytes 487,000

Leukocyte	Relative No. per 100	Absolute No. per c.mm.	Normal Blood per c.mm.
Polynuclear neutrophils	32.8	159,756	5,100
Polynuclear eosinophils	4.6	22,402	150
Polymast cells	0.6	2,922	150
Medium mononuclears	3.0	14,610	1,875
Large mononuclears	0.3	1,461	225
Lymphocytes	1.0	4,870	150
Transitional cells	0.6	2,922	150
Neutrophil myelocytes	52.8	257,136	150
Eosinophil myelocytes	3.3	16,071	150
Monomast cells	0.3	2,922	150

After Treatment, Feb. 10, 1909. Leukocytes 43,000

Leukocyte	Relative No. per 100	Absolute No. per c.mm.	Normal Blood per c.mm.
Polynuclear neutrophils	62.3	26,913	5,100
Polynuclear eosinophils	2.6	1,123	150
Polymast cells	3.0	1,296	150
Medium mononuclears	5.6	2,419	1,875
Large mononuclears	0.6	259	225
Lymphocytes	0.6	259	150
Transition cells	3.6	1,555	150
Neutrophil myelocytes	18.6	8,635	150
Eosinophil myelocytes	1.3	561	150
Monomast cells	1.3	561	150

The results of this investigation demonstrate in a most convincing manner the predilection in action of the X-rays for neutrophil myelocytes (that is, the predominating pathological elements), then for other myelocytes and lastly to a mild degree for normal elements.

Eleven cases of leukemia examined by these authors with this purpose in view demonstrate this interesting fact. A scale of sensitiveness of the blood element toward radiotherapy has thus been formulated by them as follows:

Diminution under Influence of Treatment

Neutrophil myelocytes	138.9
Eosinophil myelocytes	39.3
Basophilic myelocytes	26.2
Lymphocytes	22.8
Transitional	22.6
Polynuclear eosinophils	22.3
Medium mononuclears	21.5
Polynuclear neutrophils	16.2
Polynuclear basophils	14.2
Large mononuclears	10.9

Elischer and Engel find that the action on spleen and leukocytes continues long after treatment has been stopped.

The Leukotoxin Theory.—Irradiation of the spleen alone often suffices to get effects elsewhere. Hence arose the idea that the effect of X-rays is to produce specific leukotoxins, which are generated by the dying leukocytes and are diffusible throughout the body. The leukotoxin theory is rendered doubtful by the work of Klieneberger, Zöppitz, and Krause, who worked with every facility for bacteriological technic, but could not prove to themselves that even prolonged irradiation produced a roentgenitic leukotoxin. Yet it would seem that some indirect action (perhaps through products of decomposition) on the hemopoietic organs occurs when these organs are subjected to X-rays.

Aubertin and Beaujard insist on the leukopenia being the result of degeneration of cells throughout the whole system, and in spite of normal or increased function in blood-forming organs. It is a leukopenia due to hyperdestruction, not through insufficient formation of white cells.

It would appear that, as a result of the application of X-rays, leukolytic bodies develop. Even serum from animals treated with X-rays, when injected into another animal, causes leukopenia, as does also extract from irradiated spleen, whereas an extract of a normal spleen induces leukocytosis.

Capps and Smith have recently published a most interesting work along these lines, which seemed to show that serum of leukemic patients who were improving under X-rays caused leukopenia when injected into animals, and when added to a hanging drop of leukocytes from another individual caused disintegration of cells, especially the mononuclears; and, further, when injected into leukemic patients who had not been subjected to treatment by the rays, induced a drop in the leukocytes. Such, too, were the conclusions of Harris after treating 5 cases, in 4 of them with palliative results.

This production of leukopenia has been noted by others; thus, for example, Luca experimented with the serum of leukemic patients who had been successfully irradiated, with reduction of the leukocytes to normal. This serum was injected into other leukemic patients who had as yet not been subjected to X-ray treatment, and within two hours the white count was reduced, the maximum reduction being attained in twenty-four hours. The result, however, was temporary and later a notable increase occurred. On the basis of this observation the serum of irradiated animals was injected into animals in whom an experimental leukocytosis had been produced by turpentine, and here, too, a temporary fall in the white cells resulted, but after two days this gave place to a marked increase.

Uric Acid and Purin Bodies.—Linser and Sick reported that the X-rays cause increased uric acid and purin bodies in the urine of leukemic and normal subjects who were placed on a purin-free diet, and that the

serum from healthy men treated with X-rays when injected into healthy individuals would cause increased uric acid and leukopenia—and on this basis argued the occurrence of a roentgenitic leukolysis.

Zuccola's observations showed that, after treatment, uric acid is considerably increased, and that this may be used as a guide to treatment, for where, during radiotherapy for leukemia, a rapid diminution of uric acid occurs, the treatment should be stopped. Pseudoleukemias submitted to X-ray treatment have much less elimination of uric acid, probably because the white cell destruction is less marked.

Ambrozio claims that he has produced diminution of leukocytosis, increased excretion of uric acid, and diminution in the size of the spleen by injecting the irradiated blood-serum of a healthy man into a leukemic patient.

Vas studied more specially the elimination of nitrogen and ammonia. He confirms the current opinion which attributes the elimination of purin bodies to the destruction of the leukocytic nucleins, and he regards the increase of purin bases in the feces as a sign of grave import.

Therapeutic Effects.—The therapeutic effects of X-rays differ according to the type of leukemia.

In the *myelogenous variety* about 90 per cent are favorably affected (Taussig), though none were cured. As a rule, the spleen diminishes in size, the hemoglobin rises and the red corpuscles are usually markedly increased, the leukocytes fall (in 92 per cent of cases, Krause) and the qualitative blood picture improves, the myelocytes becoming greatly reduced and the polynuclears relatively increased, giving rise to what is known as the latent period: the rise in weight is constant, and patients improve subjectively often for months. The blood picture, however, never becomes normal, and the whole course of the disease is not greatly lengthened; when relapses occur the irradiation seems less efficacious than when used in the earlier periods of the affection. Of 187 cases of myeloid leukemia treated, 141 were much better after irradiation, and the improvement lasted for several years—the longest seven years. The remainder, chiefly old cases, were refractory.

Stengel and Pancoast found benefit in 46 out of 69 cases treated. They regarded the irradiation of the bone marrow of the whole skeleton (mapped in 8 districts and each district exposed in rotation) as being more efficacious than that of the spleen and glands. Less danger of toxic changes seemed to exist and symptoms were more easily relieved, for the seat of disease was directly attacked. The treatment requires longer time, but is more efficacious.

In some cases the treatment results in the development of an acute and rapidly fatal course, as instanced by Béclère and Béclère, in one of whose cases temporary benefit was followed by relapse with myeloblasts in the blood, characteristic of acute leukemia.

In *acute lymphatic leukemia* little improvement is obtained from radiotherapy. Minerbi and Prampolini treated one case, the white cells falling in a few days from 36,700 to 9,300, without noteworthy changes in the differential count, the lymphocytes predominating. But the red cells, on the other hand, fell too, the general condition became worse, and death occurred with hemorrhagic phenomena. During treatment there was a remarkable increase in the erythroblasts. This case was treated by the "rapid" method, which may account for the course and symptoms, for, as von Decastello and Kienbock have pointed out, this form of leukemia usually terminated by progressive leukemia and cachexia, the acute symptoms being usually lessened.

In *chronic lymphatic leukemia* the results are often striking, the glands often being reduced to the normal in two or three weeks. The leukocytes are markedly reduced, but again it is a quantitative rather than a qualitative change, for the lymphocytes remain relatively increased. Death may be delayed three to five years. Failures come through insufficient irradiation, for example, when the spleen alone is subjected to the rays. Taussig found little effect but advocated its trial in all cases.

The Technic and Mode of Employment of X-rays.—Much variation in technic exists. As a rule tubes are employed; a hardness of 6 to 7 is said to be best, measured on the Walther scale. Tubes of greater hardness cast sparks and alarm the patient; if too soft they are injurious to the skin. When a soft tube is used, the skin should be protected by an aluminum (0.5 to 1 mm. thick) or silver filter. Even with the hard tube when prolonged irradiation is applied, a filter of tissue paper, linen or chamois should be employed, and the adjacent surface should be protected by "blendenpaste"; burns are best avoided when the minimum distance of the patient from the tube is 40 cm., though this needs close attention on the part of an expert to control during the exposure.

Best results are obtained from irradiation of the long bones and spleen at frequent intervals, each exposure of short duration (five to ten minutes). The glands, liver and sternum are sometimes irradiated also.

Dosage of the X-rays is difficult because of supposed individual susceptibilities, and much is yet to be learned to acquire greater accuracy. Krause recommends from one-half to one-fourth the erythema dose at one sitting, two or three times a week, the total dose given to about equal five erythema doses.

Harris used the X-rays three times weekly for three months, then five times weekly for two months, then at longer intervals. The current was taken from the coil, and a medium hard, or a medium, tube used; sometimes a medium soft was employed. The distance from the body was 25 to 30 cm., the amperage 7 to 10, with higher tubes. Voltage, 10 to 120. Time of exposure, seven to fifteen minutes. The regions exposed

were the spleen (anterior and posterior), the thighs, epigastrium, and sternum.

Special Considerations in Use of Roentgen Irradiation.—So long as the patient shows visible signs of improvement the treatment may be continued, and especially if the leukemia diminishes, and the appetite and general condition are good.

If, on the other hand, there develops a change for the worse, perhaps with fever, diarrhea, weakness, etc., and a rapid diminution of red and white cells and hemoglobin, the treatment should be stopped.

The longer the duration of the disease the more refractory will the patient be to beneficial effects, and relapses, too, respond but little to the irradiation.

Anemias are readily induced, and they are sometimes so acute as to be dangerous, developing a condition resembling pernicious anemia and acute leukemia.

Probably a leukocytic ferment is set loose by intense leukolysis, and this acts in thermic centers, causing "radiotherapeutic fever." At all events some poison is set loose from disintegrating cells and may cause fatal intoxication.

The anemia is a guide to the dosage, in one sense, for it gives a measure of leukolysis, and implies need for cessation of the X-ray treatment. Therefore the treatment should be controlled by regular blood counts.

Only experts should use X-rays, for ignorance of the technic may readily lead to disaster.

Radium—*Action on the Blood.*—Aubertin and Delamarre, after a series of experiments on animals, concluded that the effect of radium was practically identical with that of X-rays, namely, an early, almost immediate, transient leukocytosis, followed by an essential leukopenia, which was relatively persistent. The changes could be detected sometimes at the end of one hour, and took place prior to the destruction of splenic tissue. More recently, however, the experience of many observers justifies the belief that in radium one finds a much more efficacious remedy than X-rays. Ordway, following French observers, showed this in a clinical report in 1916. Giffin, Vogel, Minot, Wood, Peabody and others testify to its superiority and have contributed valuable observations on the treatment of leukemia.

Technic.—Hard beta- and gamma-rays are employed, while the alpha and soft beta-rays are filtered out (to save the tissues) by means of a lead screen and layer of gauze. The spleen, and less often, the glands and long bones are irradiated. In the case of the spleen, the radium is exposed seriatim over various squares mapped out for twenty-four hours (3,000 mg. hours).

Effect.—There is a general improvement and increase in weight. The red blood-cells are increased, as well as the hemoglobin; the white cells

rapidly diminish, beginning about twenty-four to forty-eight hours after treatment, and they progressively decrease until, after a few weeks of treatment, the cells may attain normal number and quality, though exacerbations seem inevitable; there are fewer hemorrhages, the spleen lessens, and life is prolonged.

Thorium-X.—The therapeutic researches of Bickel and others with this radio-active element have been mentioned under Pernicious Anemia (page 826). Its effect upon the cellular elements of the blood is similar to that of radium, as set forth in the preceding paragraphs. To produce a reduction in white cells, such as is attempted in the leukemias, it must be given in much larger doses than in the anemias, where the aim is simply to stimulate the bone marrow to an increased red cell formation, and where, especially in the case of the pernicious form, large doses are both useless and dangerous. In leukemia, on the other hand, especially the myelogenous form, or in lymphomatous tumors, the treatment should be initiated by one or two large intravenous injections of one to three million maché units, followed later by daily doses by the mouth, say, of one million maché units. This treatment can be continued over some months (Bickel) without untoward effect, and has in the hands of several observers, Bickel, Klemperer and Hirschfeld, Grund, Nagelschmidt, led to marked symptomatic improvement similar to that produced by irradiation.

The Benzol Treatment.—It seems to have been Barker's discovery of the destructive action of benzol upon the blood and Selling's subsequent work on this subject which led Koranyi (1912) to use it in the treatment of leukemia and polycythemia, and subsequent observers have confirmed the efficacy of the treatment beyond any which has since been employed. Time, however, has yet to prove whether the treatment is of permanent value.

The *method of administration* now in vogue is usually Kiralyfi's. Benzol is combined with olive oil as recommended by Koranyi in doses of ½ gm. in pearls.[1] Four pearls are given on the first day during food; 6 on the second; 8 on the third day; and 10 on the fourth and subsequent days. One must begin always with small doses, gradually increasing the amount, while carefully watching the progress of the disease and condition of the blood. The individual susceptibility is decided in this way and one must proceed carefully, for latent periods often exist during which the effect of the drug is apparently nil. One should continue the use of benzol unless the white blood-cells remain at a stage much above the normal, or rise again in the course of the treatment.

The treatment should never be continued up to the time when the white blood-cells become normal, for the effects of the drug are seen for some period after the last dose has been administered. The temperature,

[1] Some patients tolerate benzol better if given in an emulsion with mucilage of acacia.—Editor.

pulse, digestion, and general condition of the patient should be carefully observed and the urine repeatedly examined.

The *advantages* of the drug are as follows: It is cheap; it is easily used; powerful in its action though not radical in its effects. It produces no dermatitis, while yet it diminishes the white blood-cells of the embryonic type, though not those of the ordinary type. The size of the liver and spleen, and glands, diminishes under the treatment. In other words, it acts very much in the same way as X-rays, and sometimes its effects are more permanent, though slower.

The *dangers* and untoward symptoms should be mentioned. The drug has toxic properties, and indiscreet use will result in headache, dizziness, nausea and vomiting, increase in the anemia and renal irritation. These symptoms or the rapid fall in the leukocyte count are danger signals, indicating the withdrawal of the drug.

Most observers agree that it is well to *combine the benzol treatment with radiotherapy,* and, moreover, that arsenic and iron should be used in the treatment just as in ordinary methods.

Duration of the treatment varies according to circumstances from three weeks to four months. Periodic courses of treatment must be undertaken.

Molczanow has treated 5 cases, with excellent results in 4. He has shown that the hemoglobin and the red blood-cells fall, to rise after a period of a week or so, and, vice versa, the white blood-cells may rise during the first week and then diminish, and that the same is true in the case of the spleen and lymph glands, which at first may increase in size and then diminish after one week. The myelocytes in his cases diminished in number while the polynuclear cells were increased. His conclusions were that the benzol destroys the pathological leukocytes, hence the leukopenia. Results of his cases showed improvement in sleep, in weight, strength and appetite, and pains in the bones were relieved. There were no relapses.

Liachowsky, Demidow, Lutschewski and Kiralyfi record cases that showed favorable results, while Turk reported one unfavorable one in which the treatment of radiotherapy succeeded better than did the benzol. Billings was the first authority in America to apply the benzol treatment in leukemia. His results in the 5 cases reported are rightly described as phenomenal. All the patients but one had previously received X-ray treatment. The benzol was usually given in gelatin capsules filled at the time of administration, beginning with 7 minims and ascending to 15 minims, three or four times daily. In all the cases there was a rapid fall in the leukocytes, amounting in three instances to a leukopenia, and preceded in two by a temporary rise. The qualitative blood picture, however, presented a bizarre mixture of many pathological types of white cells, and did not return to normal. In the 4 myelogenous cases, the red cell count and hemoglobin improved. In all 5 cases a rapid diminu-

tion in the size of the spleen occurred, much more marked than is usually seen under exposure to the X-rays, and in the 1 case of lymphatic leukemia, there was a rapid reduction also in the multiple enlarged lymph nodes. He points out that benzol, while a remedy of much promise in leukemia, should be used with caution, as its effect in large doses is certainly to render the bone marrow hypoplastic, and the danger of inducing an aplastic anemia should therefore always be kept in mind. Only the pure drug should be given, as impure benzol contains anilin and other toxic products.

Moorhead testifies to the efficacy of benzol in one case of "splenomedullary" type, and notes the suddenness of the drop in white cells (132,500 to 76,000 in three days); further the marked change in the differential white cell count. Prior to treatment, myeloblasts and myelocytes dominated the picture with 45 per cent and 10 per cent respectively, while neutrophils were relatively diminished (32 per cent). Three months after benzol had been administered the differential white cell count had returned to normal, while the red cells and hemoglobin had also vastly improved. He had less success with a case of lymphatic leukemia though, temporarily, benefit accrued.

Pappenheim looks with less favor on the benzol treatment and regards the dosage as too small to be effectual in depressing marrow cell formation. The leukopenia, he says, is only apparent, the polynuclear cells being stowed up in the internal vessels. Sohn came to the same conclusion after a study of the metabolism of benzol administration. Large doses were found to be dangerous, leading to diminished oxidation processes, acidosis and toxic necroses in the liver and kidneys.

Muhlmanns' experience confirms these observations, for a fatal result in a case of lymphatic leukemia followed the administration of 175 gm. of benzol in six months. Extensive necroses were found in the liver. Pappenheim tried benzene and found it to be equal in power to benzol and less injurious, though both were regarded as inferior to radio-active substances, and the results showed that they were neither so elective, nor radical, nor constant in their effects on the bone marrow and the hemopoietic apparatus.

Thorium, however, was found to be more potent in driving leukocytes entirely out of the peripheral circulation. Weiskotten, Schwartz, and Steensland studied the action of benzol on various groups of animals with and without splenectomy and found a temporary fall in the polynuclear leukocytes of the peripheral circulation, which they ascribed to a toxic effect.

Summary.—Our own experience has shown that benzol is a very efficacious remedy in myelogenous leukemia, reducing the size of the spleen and the number of leukocytes and improving the general condition of the patient. This improvement is only temporary, the remission lasting a

varying time up to several years. Ultimately the disease leads to a fatal issue. Sometimes the relapses are very sudden and the type changes to that of the acute lymphatic form.

Lymphatic leukemia is less influenced by benzol, but experience shows that some cases are apparently benefited by its use. Benzol indeed is ineffectual in many cases of both varieties, and experience has shown that the X-rays will often initiate an improvement where benzol has failed. Our own practice is to use them combined. Benzol may be given in gradually increasing doses commencing with 5 to 7 drops with equal parts of olive oil, in capsule, three times a day, increasing daily by 1 drop till 15 drops three times daily are used. At the same time the X-rays are used on the different parts of the hemopoietic system chiefly over the long bones and the spleen, not oftener than three times weekly. Turk and others have found cases benefited, first by the use of one method, later by the other. In one case the patient progressed favorably on X-rays alone for a time, and the treatment was then changed to benzol without effect. Recourse was then had to X-ray again with renewed benefit. In one case of chronic lymphatic type benzol was found to be useless, where the X-rays later gave great benefit. In Jespersen's case, which was of the myelogenous type, the X-ray proved useless after two courses and benzol later on proved beneficial for a time. Krokiewicz found benzol safe and not cumulative; doses larger than 3 gm. daily caused digestive disturbances and albuminuria.

The effects on the blood vary greatly in different individuals. The leukocytes do not always numerically decrease and the relation of the types of leukocytes sometimes remains as before. The effect on the viscera varies with the different cases, and no general law will be found to apply to the effects of treatment in all cases.

More often polynuclear neutrophils remain unaltered while the abnormal granular cells may diminish out of proportion to the other forms, then after a short time the preëxisting relations return.

Arsenic.—Very few drugs seem to have even a temporary effect upon this disease. It has been claimed by many that arsenic is the only useful medicine. It is given as follows:

Liquor potassii arsenitis.
Aq. amygdal amara, of each 10 parts.
Two drops three times a day, gradually increase to 30 to 40 drops three times a day for months.

Arsenic may also be given hypodermically in 1 per cent solution of the arsenic acid and distilled water; this should be boiled for an hour, and 5 parts of phenol ½ per cent solution should be added. One mg. of this should be given and increased up to 1 cg. in the same method as indicated above. Many other drugs have been employed, but with none

have there been any encouraging results. Sodium cacodylate may be used as a more intensive form of arsenical treatment, and is given intramuscularly in doses of 0.1 to 0.2 gm. every second day.

Naphthalin Tetrachlorid.—Drysdale has recently recorded a rather remarkable improvement from the use of naphthalin tetrachlorid, 8 gr. every three hours, and later every four hours. The one result is sufficiently important to render its trial interesting.

Treatment by Mixed Toxins.—Coley's serum, that is, a mixture of the toxins of Streptococcus erysipelatis and prodigiosus, has been used frequently and with perhaps slight improvement, but the results are not so encouraging as by means of the X-rays, and such was recently the experience of Larrabee, who treated 6 cases by this method and observed a slight improvement in 3 in whom arsenic had been of no benefit.

Tuberculin.—Tuberculin has also been used, but is not only useless but often dangerous.

Extirpation of the Spleen.—This has been tried, but in nearly every case fatal results ensued ultimately. Giffin is conservative as to its benefits and merely records encouragement in 6 of 26 cases. The splenectomy was done after benzol or X-ray had induced a normal blood picture. This method is, moreover, quite irrational, and takes no heed of the pathogenesis.

PSEUDOLEUKEMIA

(*Hodgkin's Disease*)

But a few words will suffice to deal with this condition from the point of view of therapeutics, inasmuch as the treatment is, in every particular, similar to that of leukemia itself. Indeed, the generally accepted view now seems to be that pseudoleukemia should be defined as an *aleukemic leukemia.* The tendency seems to be rather to regard it as a symptom, not as a disease entity, and to include it in the group of diseases which Trousseau, years ago, described as *adénie,* and which have lately been subdivided mainly into three groups, first, simple *lymphadénie,* which includes Hodgkin's disease, leukemia and similar non-malignant growths of the hemopoietic cell constituent; second, the sarcomatous form in which malignant growths characterize the malady; and, third, the granulomatous type in which the nature of the glandular involvement is that of a granulation tissue tumor.

In general it may be said that the treatment of Hodgkin's disease is unsatisfactory in the majority of cases, although cures have been recorded lasting over a period of six years, and the future would seem to be bright under modern research in treatment of this disease. The X-ray formed a prominent part in the treatment of those cases. The results vary perhaps

according to one's conception of the disease. Bunting and Yates lean towards the microbic origin of the disease and have described a polymorphin diphtheroid organism against which the body, as a rule, is unable to produce enough antibodies to overcome the infection. Some skepticism has been expressed as to the validity of this discovery. Mallory regards the disease as essentially neoplastic, not infectious, while J. H. Wright and others lay stress on the presence, normally, in the lymph-nodes, of similar bacteria. Again authors describe bacteria present also in this disease and associated with this diphtheroid organism, for example, streptococci, staphylococci, Bacillus welchii, etc. Sources of infection were looked for and the organisms were found in the tonsils and in alveolar abscesses. It is also striking, on the other hand, that the organism of Bunting and Yates has been found in lymphosarcoma. It is for these reasons that the efficacy of the vaccine produced with aërobic and anaërobic cultures, and which seem to have been followed by successful results, is to be ascribed to the concomitant treatment.

Their procedure is briefly as follows:

1. Removal of all sources of infection, for example, tonsillectomy to remove a main portal of infection; also any diseased teeth.
2. Excision of as much diseased tissue as possible.
3. Bathing the wound in iodin to prevent recurrence.
4. X-ray treatment commenced a few hours later.
5. The specific treatment by means of injecting serum or vaccine prepared from aërobic and anaërobic cultures.
6. General hygienic measures.

The success of this treatment depends, it is said, on the absence of a periadenitis. Out of 10 cases 2 were cured, up to five and six years' observation. Four others are doing well and are looked upon as ultimate cures. The remainder have not done well.

Realizing the benefit derived from X-rays alone one would seem to be scarcely in a position to attribute the success of these cases to the specific treatment per se.

Herbert French has experienced good results from the use of large doses of radium applied locally. T. R. Brown had remarkable results in 2 cases with only two applications in very large doses (200 mg.) (personal communication).

For the X-ray treatment the reader is referred to the article on Leukemia.

Arsenic is still of importance in the treatment. It is worthy of note that some of the newer preparations of Ehrlich, notably arsazetin, have been found to be of great benefit—and in 1 case, described by Naegeli, there seem to be evidences of a complete cure. The drug is given either hypodermically or by mouth. The subcutaneous injections are given as

follows: 0.6 gm. (9 gr.) subcutaneously every two days in succession, omitting the treatment for five or six days, and then repeating for two days again. By mouth one may give 0.05 gm. (¾ gr.) four times daily, watching carefully for any of the ordinary signs of intolerance from large doses of arsenic. Arsazetin seems safer and better than the newer arsenical preparations.

REFERENCES

General Articles

Pappenheim. Uber die Stellung der akuten grosszellig lymphozytaren Leukamie im nosologischen System der Leukemien u. die Bedeutung der grossen Lymphozyten Ehrlichs f. die Path. dieser Erkrankung, Folia hæmatol., 1-53, 141-201, 329-388, 535-602, 1907.

——— Zur Therapie u. z. differential Diag. der makrolymphozytaren Leukamie, Synop., Folia hæmatol., x, 1, July, 1910.

Radiotherapy

Ambrozio. Action of Röntgenizer Serum on Experimental Leukocytosis, Gior. Internaz. d. sc. med., 18, 1908. Synop., Arch. d. mal. du cœur, March, 1909.

Aubertin et Beaujard. Sur le Mechanisme de la Leucopénie Produite experimentalement par les Rayons X, March 7, 1908. Synop., Arch. d. mal. du cœur, 655, 1908; 325, 1914.

Béclère and Béclère. Une Nouvelle Indication Prognostique au Cours du Traitement des Leucémies Myeloides par les Rayons X, Cong. Internat. de Physiothér., Paris, 1910.

Béclère and Bulliard. Variations Leucocytaires dans la Leucémie Myeloide sous l'Influence des Rayons de Roentgen, Rapport de Sensibilité des differents Eléments à l'Action de ces Rayons, Echelle de Sensibilité, Soc. de radiol. méd. de Paris, April, 1909. Synop., Arch. d. mal. du cœur, Nov., 1909; also Folia hæmatol., July, 1910.

Capps, J. A., and Smith, J. B. Experiments on the Leukolytic Action of the Blood Serum of Cases of Leukemia Treated with the X-ray, and the Injection of Human Leukolytic Serum in a Case of Leukemia, Journ. Exper. Med., ix, 51, 1907.

Demieville. Presse méd., 1er Aout, 1914. Synop., Arch. d. mal. de cœur, 357, Oct., 1915.

Desplats. Radiother. in Myeloid Leukemia, Cong. Internat. de Physiothér., Paris, 1910. Synop., Arch. d. mal. du cœur, 20, 85, 1908.

Desplats. Voluminous Lymphadenoma Treated by X-rays, Journ. de Sc. méd. d. Lille, May 22, 1909. Synop., Arch. d. mal. du cœur, 62, Jan., 1910.

Dupeyral. Radiotherapy in Adenitis, Marseille méd., April 15, 1909.

Elischer and Engel. Radiotherapy in Diseases of the Blood, Ztschr. f. klin. Med., lxvii, 31-67, 1909.

Harris. X-ray Treatment of Myelogenous Leukemia, Am. Journ. Med. Sc., 78, 1908.

Heinecke. Mitt. aus d. Geb. d. Med. u. Chir., xiv, 1 and 2, 1909.

Houde. Le Traitement de la Leucémie Lymphatique par la Radiothér., Thèse de Paris, 1910.

Krause. Munchen. med. Wchnschr., No. 42, 1904. Review of Literature, Schmidt's Jahrbuch, July, 1913.

Krone. Munchen. med. Wchnschr., No. 21, 1904.

Linser et Sick. X-rays and Urinary Purins, Deutsches Arch. f. klin. Med., lxxxix, 413, 1908.

Luca. Action of Serum of Animals Treated by X-rays on Experimental Leukocytosis, Arch. di farmacol. sper., 1, 1907. Synop., Arch. d. mal du cœur, 317, 1908.

Ménétrier et Touraine. Étude de l'Action Histologique des Rayons de Roentgen dans la Leucémie Lymphoide, Arch. d. mal. du cœur, Feb., 1911.

Mimerbi et Prampolini. Effects of Radiotherapy in Acute Leukemia with Small Lymphocytes, Priv. Crit. di Clin. Med., April 13, 1907. Synop., Arch. d. mal. du cœur, 327, 1908.

Oettinger, Fessinger et Sauphar. Des Anémies et des Processus Leucolytiques Survenant dans les Leucémies au Cours du Traitement Radiothérapie, Arch. d. mal. du cœur, 273, May, 1910. Synop., Folia hæmatol., July, 1910.

Pirie. Radiotherapy in Tuberculous Adenitis, Brit. Journ. of Tuberc., April, 1908. Synop., Arch. d. mal. du cœur, Jan., 1910.

Pribam u. Rosky. Ztschr. f. exper. Path. u. Therap., vi, 7-24, 1909. Synop., Folia hæmatol., July, 1910.

Pusey. Journ. Am. Med. Ass., Sept. 28, 1902.

Stengel and Pancoast. A New and More Rational Method of Treatment by X-rays, Journ. Am. Med. Ass., April, 1908.

Taussig. Interstate Med. Journ., xv, 439, 1908.

Vas. Changes in Irradiated Leukemias, Ztschr. f. klin. Med., lxix, 1909.

von Decastello u. Kienbock. Fortschr. a. d. Geb. d. Rontgenstrahlen, xi, 1907, p. 377. Synop., Arch. d. mal. du cœur, 327, 1908.

Warthin, A. S. An Experimental Study of Effects of Roentgen Rays Upon the Blood-forming Organs, with Especial Reference to the Treatment of Leukemia, Internat. Clin., iv, 243, 1906.

Warthin, A. S. Comparison of Roentgen Irradiation and Administration of Arsenic in Treatment of Leukemia, Internat. Clin., 1907.

——— Phys. & Surgeon, Jan., Feb., and Mar., 1907, gives full summary of literature to date. Synop., Folia, hæmatol., viii, 1, 1909.

Warthin. Les Modifications des Tissues Leucaemugnes Productes par Leur Exposition aux Rayons X, Arch. d'electric. méd., March 25, 1914.

——— Synop., Arch. d. mal. du cœur, 260-265, August, 1915.

Ziegler, Kurt. Clin. and Hist. Results of Isolated Irradiation of Spleen by X-rays, Ztschr. f. Med., Elektrol. u. Roentgenk., March, 1909.

——— Ztschr. f. klin. Med., xxii, 1, 2, 1893.

Zuccola. Uric Acid Elimination in Leukemia Treated by the X-rays, Rassegna di terap. 20, 1908. Synop., Arch. d. mal. du cœur, March, 1909.

Radium and Thorium-X

Aubertin et Delamarre. Action du Radium sur le Sang, Soc. de biol., Mar. 14, 1908.

Bickel. Thorium-X in Anemia, Leukemia and Rheumatism, Berlin klin. Wchnschr., Feb. 24, 1913.

Dominici et Barcat. Action de Radium sur le Tissue Conjunctive-vasculaire, Arch. d. mal. du cœur, 153, 1908.

French. Medical Annual, 379, 1916.

Grund. Thorium-X in Leukemia, Munchen. med. Wchnschr., 1175, 1913.

Klemperer and Hirschfeld. Weitere Mittheilungen über die Behandlung der Blutkrankheiten mit Thorium-X, Therap. d. Gegenw., No. 54, 57, 1913.

Meseth. Therapeutic Use of Thorium-X, Munchen. med. Wchnschr., Sept. 23, 1913.

Nagelschmidt. Thorium Treatment of Leukemia, Deutsche med. Wchnschr., 1830, 1912.

Pappenheim and Plesch. Experimental and Histological Investigations into the Action of Thorium-X on the Organs and on the Hemopoietic Apparatus, Folia hæmatol., xiv, 1, 1912.

Benzol-Therapy

Aubertin and Parvu. Benzol in Leukemia, Presse méd., 442, 1913.

Billings. Benzol in Leukemia, Journ. Am. Med. Ass., Feb. 15, 1913.

Blick. München. med. Wchnschr., 1176, 1913.

Demidow. Chronic Myeloid Leukemia Treated by Benzol, Russk. Vrach., No. 11, 1913; Synop., Folia hæmatol., July, 1913.

Jespersen. Benzolbehandelter Leukämia mit eigentumlichem Verlauf, Deutsche med. Wchnschr., July 3, 1913.

Kardos. Benzol in Leukemia, Budapesti orv. ujság., xi, 45, 1913.

Kiralyfi. Benzol in Leukemia, Wien. Klin., xxv, 1311-1318, 1912.
Klein. Wein. klin. Wchnschr., No. 26, 357, 1913.
Koranyi. Ibid., xxvi, 125, 1913.
Krokrewicz. Ibid., 1913.
Liachowsky. Treatment of Leukemia w. Benzol, Russk. Vrach., No. xii, 1913; Synop., Folia hæmatol., July, 1913.
Lutschewski. Benzol Treatment of Leukemia, Folia hæmatol., July, 1913.
Meyers and Jenkins. Albany Med. Ann., July, 1913.
Molczanow. Brit. Med. Journ., March 6, 1915.
Moorhead. Ibid., March 6, 1915.
Muhlmann. Deutsche med. Wchnschr., xxxix, 1913.
Pappenheim. Wien. klin. Wchnschr., No. 2, 48, 1913.
Rodelius. Artzl. Ver. in Hamb., June 3, 1913.
Rosler. Wien. klin. Wchnschr., No. 21, 1913.
Selling. Purpura Due to Benzol, Johns Hopkins Hosp. Bull., 33, 1910.
Sohn. Wien. klin. Wchnschr., April, 1913.
Stein. Ibid., No. 25, 1938, 1912.
Stengel. Retrospect of Literature on Diseases of the Blood, Progressive Medicine, 327, June 1, 1913.
Türk. Wien. Gesell. d. Inn. Med., Jan., 1913.
Wachtel. Deutsche med. Wchnschr., Feb. 13, 1913. Abstr. in Journ. Am. Med. Ass., March 22, 1913.
Weiskotten, Schwartz, and Steensland. Journ. Med. Res., Sept. 15, 1915.

Arsenic, Arsazetin, Atoxyl

Cohnheim. Kasuistischer Beitrag. z. Anwenden des Atoxyls bei Leukemia, Med. Klin., 41, 1907; Synop., Folia hæmatol., viii, 1, 1909.
Dickson. Case of Leukemia Successfully Treated with Arsenic, Lancet, 1906.
Naegeli. Uber die Behandlung Pseudo-leukamischen Affectionen mit Arsazetin, Therap. Monatsh., Feb., 1910.

Mixed Toxins

Larrabee. Treatment of Leukemia, Bost. Med. & Surg. Journ., Feb. 6, 1908; Synop., Arch. d. mal. du cœur, 1908.

Vaccine Treatment of Hodgkin's Disease

Bunting and Yates. Bost. Med. & Surg. Journ., Dec., 1915.

CHAPTER XXXVII

BLOOD DISEASES WITH CYANOSIS

C. F. Martin

POLYCYTHEMIA WITH SPLENOMEGALY

Synonyms.—Polycythemia rubra megalosplenica; Osler-Vaquez' disease; erythremia; primary myelogenous polycythemia megalosplenica; true idiopathic polycythemia.

Polycythemia has hitherto been regarded as a primary disease of the blood-forming organs; the condition is in all likelihood a syndrome associated with various and many causes, and sometimes associated with hypopituitarism. There is a hyperplasia and increased function of the bone marrow, leading to a marked increase in the number of red cells, and frequently to secondary enlargement of the spleen. The essential pathognomonic feature is the cyanosis resulting from an increase in the total number of red corpuscles. With this, however, there is an increased blood volume and splenic enlargement. New microscopic methods have proved a widening of vessels in the skin, with mechanical destruction and increased viscosity of the blood. Clinically, it is characterized by a cyanosis and splenic hypertrophy, developing progressively and insidiously, as well as certain functional troubles dependent on a peripheral or visceral blood plethora. There are usually some fullness in the head, epistaxis, vertigo and intermittent albuminuria. Two types occur:

1. *Physiological* polycythemias occurring in high altitudes and sea climates, in the newly born, etc., and

2. *Pathological,* those secondary pathological polycythemias as are present in congenital heart disease, in hypertension (Geisbock), in poisoning by phosphorus, etc., and those conditions of lessened blood plasma, through marked loss of fluids, such as occur in profuse vomiting, diarrhea or sweating, or in diabetes insipidus.

Ayerza's Disease.—Again, there is a condition described by Ayerza, and emphasized by Warthin, in which a polycythemia is associated with luetic pulmonary arteries. This so-called "cardiacos negros" has symptoms

other than those usually found. There is somnolence, ordinarily hemoptysis, and marked enlargement of the right heart.

Historical Note.—The condition was first described by Vaquez in 1892, and then by Rendu and Widal in 1895. In 1903, Osler recorded 4 new cases in addition to those referred to by him as already reported, and he confirmed the view that the condition should be regarded as a new clinical entity. Türk followed with 7 personal observations added to the 14 which he was able to collect from the literature, and Senator in 1911 made a careful up-to-date review. Richards and Herrmann associate the condition with increased cholesterol content of the blood-serum due to impaired liver function; as a result, red cell destruction is inhibited. Engelking draws attention to the familial nature of the malady, in one instance through three generations, the present family exhibiting the disease in five brothers and sisters.

Geisbock's Disease.—This name is given to a condition of polycythemia with hypertension, arterial sclerosis and nephritis, and which Senator himself recognized as a variety of the disease (polycythemia hypertonica). A clinical description of the two forms is given by Monroe and Teacher.

Symptomatology.—The disease usually occurs in the fourth and fifth decades. Weakness, vertigo, headache, and other signs of cerebral congestion usually coexist with a chronic cyanosis moderate in degree, which is of long standing and development. There may even be local paralysis, paresthesias, hemianopsia, and other disturbances of vision. Brain lesion has been suspected. The abdomen is enlarged, corresponding to the degree of splenomegaly, and there may be a history of hemorrhages from the internal organs, while the skin and mucous membranes show a bluish red mottling.

Tachycardia is frequent. The blood changes are characteristic, the erythrocytes being increased to eight, ten, or even thirteen million, and the hemoglobin rising in some cases to 200 per cent. A moderate leukocytosis, ten to twenty thousand, is the rule, but the differential count is not characteristic of any abnormality. The total volume of the blood is increased and its oxygen content, as well as the respiratory interchange of gases, is much raised. Blood-pressure is usually not elevated, nor is there cardiac hypertrophy. The urine may be normal, or may contain urobilin.

Pathogenesis.—Senator ably discusses the various explanations of the polycythemia which have been given. He dismisses the theory of its origin from a lessened destruction of the erythrocytes, by the hyperplasia of bone marrow, which is always present, and the increased excretion of iron in the urine which is frequently present. Against the possibility of its being a compensatory process in insufficient oxygenation, he points out that the oxygen content of the blood is abnormally high, and the

heart's action usually increased. Thus it can only be due to a *primary increased functioning of the bone marrow leading to increased hemopoiesis.* That the spleen does not play a leading part is proved by the fact that splenectomy does not cure the polycythemia, which has been known to set in *after* splenectomy.

Treatment.—The treatment until recently has been unsatisfactory, and indeed, except in a very few instances, but little can be said of it, for almost no positive results have been obtained; the cases usually progressing slowly downward, through a duration of some six to eight years, to death. *Splenectomy* has been proved ineffectual and has no rational basis, the enlargement of the spleen being evidently not the primary cause. Wagner reports 3 cases of polycythemia, 2 of which were associated with splenomegaly, in which repeated venesection with removal of 300 c.c. to 350 c.c. of blood was practiced with good effect upon the subjective symptoms, especially the very severe perspiration. *Venesection* for the relief of the congestive symptoms resulting from the plethora has been found useful, but as a temporary measure only. *Oxygen inhalations and internal administration of potassium iodid* have given only negative results. Weber recommends these measures as palliative in the secondary polycythemia with cyanosis of chronic heart disease.

Repeated application of X-rays, in conjunction with benzol therapy (15 ♏ to 1 dram t.i.d.) may be said to be the only measure that has been attended with any degree of success. Barker and Irwin have reported some rather remarkable results, and Forschbach had moderate success with similar methods, and emphasizes the need of avoiding any leukopenia during treatment. Béclère claims excellent results by irradiation alone, restricting the treatment to the humeri, femurs and the sternum. Bottner's experience is similar. He recommends treatment over the bones to paralyze the erythropoietic action. On the other hand, he also irradiates the splenic area to promote erythrolysis, and Falta has had a similar view.

Of other treatments, the only noteworthy experience is that of Eppinger and Kloss, who lay stress on the value of phenylhydrazin and toluylendiamin. The phenylhydrazin was administered subcutaneously in doses of 2 to 10 c.c. of a 1 to 5 per cent solution.

ENTEROGENOUS CYANOSIS

This is a rare condition, characterized clinically by a peculiar bluish discoloration of the skin and mucous membranes without dyspnea or any of the other signs of circulatory disturbance usually present in cyanosis, and unassociated with any lesion of the heart or lungs. The pathological change exists in the blood itself, which is of a dark-colored, venous hue, and presents, on spectroscopic examination, the characteristic absorption

bands of methemoglobin or sulphhemoglobin. The blood count may be normal and there is no polycythemia. Digestive disturbances, evidenced by obstinate constipation or protracted diarrhea, are usually present and are looked upon as having an etiological relation, the process being believed to be an *autotoxic enterogenous* cyanosis (Stokvis). This is supposed to be the result of the absorption of poisonous products from the intestinal canal, and analogous to the methemoglobinemia produced by poisoning with the anilin dyes, etc.

Treatment.—As the two forms of enterogenous cyanosis appear to differ somewhat in their etiology, the treatment must be considered separately, although, in the present state of our knowledge, little authoritative can be said.

Autotoxic Methemoglobinemia.—This is usually associated with intestinal disorders, chiefly diarrhea, and sometimes with the presence of animal parasites. The patients usually complain of headache and weakness of the limbs. The characteristic cyanosis may persist over years, varying in intensity from time to time, and often leading in the end to slight clubbing of the fingers, although the blood count may remain normal. The urine shows no methemoglobin, but the ethereal sulphates and the indican are increased, while bacteria and putrefactive products abound in the feces and point to the intestinal contents as the source of the disease. The condition may possibly be due to some element in the diet, for in some of the cases marked variations in intensity followed upon alterations in this. Thus, in van der Bergh's case, the cyanosis disappeared completely on an exclusively milk diet, to return with great intensity when a meat diet was resumed.

Thorough intestinal antisepsis, combined with a milk diet, or one poor in proteins and consisting chiefly of milk and milky foods, is thus the only regimen that can be laid down in the present state of our knowledge. This was successful in Gibson and Douglas' case, the blood becoming sterile, and the cyanosis improving.

Sulphemoglobinemia.—Cyanosis from this cause may last also for years. Wynter's case had a duration of twelve years. The symptoms are identical with those of methemoglobinemia, except that constipation is the rule, the blood is usually sterile, and the urine is normal as regards indican and sulphates. The pathogenesis of these cases is not easy to determine. From the nature of the clinical compound the cyanosis is evidently due to chronic poisoning with SH_2, and yet, in this condition, one does not always find this gas increased in the intestine. It has been suggested that in some unexplained way conditions in the intestine may be favorable to increased absorption of this gas. In this connection, and from the point of view of treatment, van der Bergh's case is again very instructive. The patient, a boy of nine, had had since birth a urethrorectal fistula following operation for imperforate anus. Through this fistula feces and

decomposed urine were mixed in the rectum and were there retained. The free exit of feces and passage of the urine through the normal channel were permitted by dilatation of the rectum and by the retention of a catheter in the urethra, and these measures were immediately followed by improvement. Thus, in this case, cure followed the relief of constipation.

REFERENCES

Polycythemia with Splenomegaly

Béclère. Le Traitement de l'érythrémie ou maladie de Vaquez à l'aide des Rayons Roentgen, Bull. Acad. de méd., lxxxvii, 227, 1922.

Bottner. Deutsche med. Wchnschr., xlvi, 1920.

Collins. Chronic Cyanosis of Extremities with Polycythemia and Splenomegaly, Med. Rec., November 21, 1903.

Engelking, E. Uber Polyzythämie als vererbbare Störung der inneren Sekretion, Deutsche med. Wchnschr., xlvi, 1140, 1920.

Eppinger and Kloss. Therap. Monatsh., xxxii, 1918.

Falta. Wien. klin. Wchnschr., xxxii, 1919.

Forschbach. Berl. klin. Wchnschr., 1034, 1919.

Monro and Teacher. Three Cases of Polycythemia, Lancet, London, i, 1015, 1913.

Osler, W. Chronic Cyanosis with Polycythemia and Enlarged Spleen, Am. Journ. Med. Sc., August, 1903.

——— Discussion of Splenic Enlargements Other than Leukemic, Brit. Med. Journ., October 17, 1908.

Richards and Herrmann. Polycythemia Vera, Minn. Med., iv, 161, 1921.

Senator. Polycythemia and Plethora, Festschr. z. Feier d. 50-jähr. Besteh. d. med. Gesellsch., 1911; Synop., Folia hæmatol., Dec., 1911.

Türk. Beiträge zur Kenntniss des Symptomenbildes Polycythämie mit Milztumor und Cyanose, Wien. klin. Wchnschr., 6, 7, 1904; Synop., Folia hæmatol., 425, 1904.

Vaquez. On a Special Form of Cyanosis Accompanied by Excessive and Persistent Polyglobulemia, Soc. de Biol., May 7, 1892.

——— Modifications of the Blood in Chronic Cyanosis, Soc. de Biol., March 2, 1895.

Vaquez and Laubry. Cyanose avec splenomegalie et polyglobulie, Bull. et mém. Soc. méd. d. hôp. d. Paris, July 24, 1904.

Wagner. Venesection in Polycythemia, München. med. Wchnschr., No. 60, 408, 1913.

Weber. Secondary Polycythemia and Heart Disease, Arch. d. mal. du cœur, 225, April, 1913.

Enterogenous Cyanosis

Garrod. Enterogenous Cyanosis, Allbutt and Rolleston's System of Medicine, v, 838-845, 1919.

Gibson. Additional Observations on Microbic Cyanosis, Quart. Journ. Med., Oxford, i, 29, 1908.

Gibson and Douglas. Microbic Cyanosis, Lancet, ii, 1906.

Hymans van der Bergh, A. A. Enterogene Cyanose, Deutsches Arch f. klin. Med., lxxxiii, 86, 1905.

Stokvis. Nederl. Tijdschr. v. Geneesk., Amst., 1902. Quoted by Garrod.

Talma, S. Intraglobuläre Methämoglobinaemie beim Menschen, Berl. klin. Wchnschr., xxxix, 865, 1902.

West and Clarke. Idiopathic Cyanosis Due to Sulphhemoglobinemia, Lancet, i, 272, 1907.

Wynter, W. Essex. Proc. Royal Soc. Med. (Clin. Sec.), i, 48, 197, 1908.

CHAPTER XXXVIII

HEMORRHAGIC DISEASES

C. F. Martin

PURPURAS

By purpura is meant a disorder of the system in which spontaneous hemorrhages arise in the skin and from the mucous membranes. It is, perhaps, more correct to regard it in the light of a symptom rather than a disease. The original disease, purpura hemorrhagica—described in 1775 by Werlhof, and known as morbus maculosis—was regarded as a clinical entity, but since then many subdivisions of purpura have been described.

Classification.—Every classification hitherto submitted has been unsatisfactory for one reason or another, all the more so as the etiology of the disease is by no means clear. Hemorrhagic diseases are difficult to group. In addition to the ordinary idiopathic purpural hemorrhage, there is an idiopathic purpura allied to the erythemas and to angioneurotic edemas. In these cases cutaneous hemorrhages alone occur. The essential feature seems to be a deficiency of blood-platelets. There are immature red blood-cells and white blood-cells, but the activity of the bone marrow does not seem to be much impaired. The coagulation time is variable. Then, too, there are the so-called primary hemorrhagic diseases, in which no blood defect is evident.

The idiopathic purpuras are sometimes mild, and at other times severe, and for the most part the causes are undetermined. To the milder forms, the term "simple purpura" is usually given, while to the severer forms, with hemorrhages from the mucous membranes, various names are given, such as "purpura hemorrhagica," "idiopathic paucity of blood-platelets," "pseudohemophilia," "essentielle thrombopenie." In some types of purpura joint pains develop, and these cases have been described as purpura rheumatica or Schönlein's disease (peliosis rheumatica). The term applies more to the senile forms but is confusing. In still another set of cases, purpura arises with prodromata, with digestive disturbances, joint pains, general malaise and swelling of the spleen (Henoch's purpura),

The different types of purpura vary in degree, in extent, in localization and in intensity. The secondary purpuras arise in many infectious diseases, typhus, typhoid fever, cerebrospinal fever, general sepsis, the exanthemata, lues, cholera, etc., as well as after intoxication (snake bites, blood poisons, etc.). They are, moreover, not infrequent in cachexia, in certain nervous conditions, and as a result sometimes of mechanical causes.

Purpura Hæmorrhagica.—The clinical picture of this disease may be mild or severe, acute or chronic, congenital or acquired. Sometimes it is intermittent and very chronic, as in a case under C. F. Moffatt's care, where the purpura recurred at frequent intervals over several years, benefit in most attacks resulting from transfusion. Hemorrhages appear in the skin, and may vary in size from minute petechiæ to large effusions under the deeper layers of the skin. These purpuric spots appear on the trunk or on the extremities, preferring the extensor surfaces. Their color varies and they go through all stages from a brown-red color to a blue, green, yellow, until finally the normal color of the skin returns. There may be one or more crops in the severer forms of the disease, the spots appearing not only superficially but deep down in the subcutaneous tissue and in the muscles. The mucous membranes may also bleed, and sometimes hemorrhages occur from nearly all the mucous surfaces, and the disease may run a fatal course. Large hemorrhages may thus occur from the bladder, or the kidneys, from the intestines, from the stomach, from the uterus and from the lungs, imperiling the life of the patient from sheer loss of blood. Sometimes wheals occur, the so-called purpura urticans.

The prognosis should always be guarded. In children, sometimes, the terminal stage is ushered in by intracranial bleeding.

Pathogenesis.—Since the interesting researches of Duke and others it has been generally conceded that purpura is directly associated with a deficiency in blood-platelets. Normally about 200,000 to 400,000 exist in the blood to each cubic millimeter while in purpura hemorrhagica there may be 10,000 or even less ("essential thrombopeny"). It is perhaps still uncertain whether this be the cause or effect of the disease and it is not decided to what extent changes in the vessel wall may contribute to the picture. The platelets or some substances produced by them are important where irritant chemical or bacterial toxins enter the blood-stream. During normal coagulation platelets disintegrate. In hemorrhagic diseases they should form a nidus from which fibrin extends in the formation of a clot. No doubt other changes occur too, and we have to do with the amount of circulating antithrombin, prothrombin and calcium, but the exact disturbance is still unknown. We do know that in purpura hemorrhagica a clot does not retract, and that it does not extrude serum; further, that the coagulation time is not prolonged (thus differing from the hemophilic state), and lastly that the bleeding time of a needle prick is lengthened.

Treatment.—Where possible the cause should be found and treated. Prophylaxis is useless to attempt except in so far as relapses are known to occur, and everything possible should be done to avoid this event. Except in the very mild cases, rest in bed is essential. The patients should not be allowed to move in bed, and the bedding should be made as smooth and unruffled as possible, for anything tending to cause injury to the skin is liable to induce hemorrhages in that spot. The air of the room should be cool, and the patient should be kept quiet. The diet should be of the ordinary plain, nourishing variety, milk being especially useful, perhaps on account of its calcium content. Stimulants should be avoided. In the treatment of purpura, as in all the hemorrhagic diseases, the methods of transfusion and of serum therapy are of paramount importance.

Transfusion (*See Pernicious Anemia*).—Transfusion seems to be the ideal method of treatment inasmuch as the transfused blood supplies the defective substances, namely, the platelets, and usually checks the hemorrhage promptly.

By Levine's rapid method of testing compatibility of the donor, one may carry out the treatment with promptitude. It is important to transfuse early, and in large quantities, in order to raise the supply of platelets which are responsible for stopping the hemorrhage. The transfusion should be repeated for the effects are very brief. The reason for this is that the new platelets remain increased for perhaps only a short period of a few days. The results of transfusion are more satisfactory in the acute and subacute cases, though sometimes even in these the transfusion of the blood into the vessels resembles in its effect that of pouring fluid into a sieve.

Emsheimer used whole blood subcutaneously and intramuscularly in doses of 20 c.c. and obtained satisfactory results. The method is simple, safe, effective and has no untoward results. Howard recorded a similar experience, and Jarvis in the pediatric clinic at Hartford preferred this to all other methods. He took the blood from a convenient vein of some relative by means of a record syringe, injected from 10 to 20 c.c. into the buttocks of the child, repeating the dose in four or six hours. Ottenberg and Libman treated 9 cases successfully.

Serum Therapy.—The effect of serum therapy seems sometimes almost equal to that of transfusion. The normal serum of the horse or rabbit has given excellent results. Ten to 30 c.c. may be injected into the subcutaneous tissues, or one may give a smaller dose, up to 10 c.c., intravenously, and repeat after a few hours or more, according to the severity of the case. In the milder cases, the injection may be repeated every second day for three days, and no longer. There is some danger of anaphylaxis if the injections are repeated within eight or ten days. This, of course, is not the case with human serum, for no danger exists with human blood. The writer can testify to these benefits in a number of

cases, and would recommend larger doses, say 20 c.c., repeated on several successive days. The satisfactory results attending the use of the serum treatment are particularly well described by Weil. Cases illustrating three types may be mentioned as of interest.

Acute Purpura.—Acute purpura was successfully treated in the case of a woman whose symptoms were those of febrile polyarthritis, gastric disturbances, spongy bleeding gums, and epistaxis, and later on subconjunctival and cutaneous hemorrhages and marked hematuria.

The condition lasted one week, and the blood, on examination, showed marked diminution in coagulability. Fifteen c.c. of fresh bovine serum were given intravenously with marked improvement next day, and the disappearance of the fever, the joint pains, and the hematuria. One week later there was slight recurrence of all the symptoms, but in five days the patient's condition became normal, and she left the hospital with no signs of illness other than slight diminution of the blood coagulation-time.

Posttyphoidal Purpura Hæmorrhagica.—This case occurred in a man with fever, ecchymoses, melena, hemorrhagic gingivitis, and hematuria, lasting three days. Thirty c.c. of antidiphtheritic serum were administered hypodermically, and within two days all symptoms had disappeared.

Chronic Purpura.—A man, aged 42, an alcoholic, showing enlargement of the liver, joint pains, and purpura of the arms and legs for months, had likewise continuous hematuria. It was also noted that all cuts remained bleeding for an abnormally long time. With care he improved and gained 25 pounds, but the purpuric conditions persisted. Bovine serum was given intravenously, and repeated in a week, when all the symptoms disappeared, and 8 months later he was still well. Nevertheless, another 15 c.c. of serum was administered, and when seen 8 months later no further purpura had occurred, even though he had resumed his alcoholic habits.

Coagulen (*Kocher-Fonio*).—An extract of animal blood-platelets, prepared as a yellow powder, soluble in water, is used intravenously and subcutaneously; 1 gm. in 10 c.c. aq. dest. supplies one of the defects, but lacks the freshness of ordinary serum (Halpen). It is of greatest use as a local styptic. Frank centrifugalized human blood-plasma, extracted the blood-plates and used them locally and intravenously with good results.

HEMORRHAGIC DISEASES OF THE NEWBORN

In this disease the bleeding may occur from the navel, from the alimentary canal, mouth, stomach, or rectum, or from the nose, bladder, etc. It is usually accompanied by jaundice.

Two conditions are recognized under the title of "hemorrhagia neonatorum," the one associated with syphilis and sepsis, the other a distinct

entity in that so far no etiology has been found. To the latter has been assigned the name "morbus maculosis neonatorum."

Treatment.—Two forms of treatment have been recommended, the one by *serum injections,* which as a rule is most satisfactory; the other by *indirect transfusion.* The former is preferable as being more easily carried out, for indirect transfusion is difficult in these cases on account of the infantile condition of the patient. Lespinasse had 13 recoveries out of 15 patients with hemorrhagia neonatorum treated by direct transfusion. (For details of these two forms of therapy see under Hemophilia.)

Unger's results are remarkable. Nine out of 10 cases recovered. Transfusion was carried out through the medium of the basilic vein in preference to the longitudinal sinus, which he regarded as dangerous. Vincent considers transfusion beneficial chiefly in the severer types and prefers serum treatment for other cases. In 31 patients, there were only 4 deaths.

HEMOPHILIA

Hemophilia may be defined as a diathesis, hereditary or otherwise, characterized by a predisposition to hemorrhages which are either induced or spontaneous. The disease is probably exclusively confined to males and transmitted only through females. (Cases occurring in women are probably some form of chronic purpura.) Hemorrhage induced by the slightest wound is the chief factor, while the spontaneous hemorrhages are of secondary importance, and are often indeed hard to differentiate from certain forms of chronic purpura. Clinically three features are of importance: (1) hemorrhages occurring after a cut, fall, pinch, or other injury, sometimes with an endless flux of blood that endangers life; (2) spontaneous hemorrhages from the skin, mucous membrane, viscera, and muscles; and (3) hemorrhagic swellings over and about the joints.

According to some authorities two types of hemophilia are described: (1) Familial, which is hereditary, transmitted by women, and occurring chiefly in males. This form occurs from earliest infancy, and the victims die from hemorrhage usually in early adult life, rarely reaching advanced age. The blood in this variety is abnormal in several ways and is thought to contain an anticoagulative body. (2) The second type, the isolated or sporadic, is an attenuated form and appears to be accidental and without hereditary predisposition. The tendency is revealed, however, in the slightest wound, but the bleeding is usually much less serious. In this variety it is said that the blood, which seems normal, has no coagulative ferment. Analogous to this second variety are the hemophilic states, so-called, which exist in hepatic, renal, and certain infective and toxic diseases.

Etiology.—The cause is still shrouded in mystery, the one fact remaining, namely, the incoagulability of the blood or its delayed coagulation. Recent observers insist on a deficiency of prothrombin as a constant characteristic, or that there may occur abnormal amounts of heparin, the antiprothrombin substance which, if increased, might induce slow activation of prothrombin into thrombin (Howell). Hurwitz and Lucas, studying problems of blood coagulation in hemophilic states, conclude that the reaction of hemophilic blood is normal, and that while coagulation is delayed the clot once formed shows normal retraction. Further that circulating prothrombin is the essential defect, while the other two factors in clotting, namely, antithrombin and fibrinogen, are normal. Whether or not, however, this is due to insufficiency of the thrombokinase, a film-forming substance secreted by the vessel wall, as Sahli thinks, or whether, again, it be an imperfection of the thrombozyme, through insufficiency of the wall and leukocytes (Nolf and Herry), is not determined. P. E. Weil regarded the mechanism of hemophilia as being due, in the sporadic cases, to an insufficiency of plasmase secreted by the leukocytes, while, in the hereditary form, there was sufficiency of the plasmase, but the presence of anticoagulants. Labbé sums up the matter by saying that incoagulability alone is not the cause, that there exist a friability and some generalized loss of function of the vessel wall, some chemical process occurring which prevents coagulation.

More recently Fonio and Minot and Lee have studied the blood-platelets in relation to hemophilia, and believe that some prothrombin substance is defective in quality rather than in quantity; that this antecedent substance, whatever be its nature or its defect, has a definite relation to the platelets—their slow availability for coagulation. Transfusion in hemophilia seems to prove this theory, for it induces a normal clotting time in the hemophilic blood for as long a time as the duration of the introduced platelets.

Symptoms.—Bleeding is the chief feature. It is rarely, if ever, spontaneous and is usually due to a trauma, though it does not occur from pin-pricks. According to Pratt, the amount and persistence of the bleeding are more important than its occurrence. Hence there is no danger in examining blood in this way for hemophiliacs. In other words, the bleeding time of hemophiliacs is normal. The mucosa, the joints, the gums and the kidneys are commonly involved. Unexplained variations in intensity occur, and the first hemorrhage is rarely fatal.

Diagnosis.—The differential diagnosis concerns chiefly the family history, and a differentiation from chronic purpura; in the latter, the platelets are always diminished.

Prognosis.—True hemophiliacs do not usually attain adult life, or, if they do, hemorrhage or joint troubles are apt to be recurrent.

Treatment may be described as general and normal.

General Treatment.—Diet is scarcely of importance, though one recommends victims of this disease to avoid substances that raise arterial tension, such, for example, as alcohol, tea and spices. Milk is recommended because of its calcium content, and especially if the blood loss be excessive.

It is of the utmost importance that time should not be wasted with drugs that are known to be useless, for many a life is lost in that way. As a matter of fact, however, bleeding in most hemophiliacs stops eventually; therefore simple methods should be tried at the outset. Locally, one may employ a ligature if necessary. In other cases, the application of some coagulant, like coagulose, cephalin, etc., meets with success. Should these fail the next step is the use of general hemostatics; the simplest of these is undoubtedly some form of blood-serum, freshly prepared. If this is ineffective, it may be necessary to transfuse, and every hemophiliac should have a list of suitable available donors. The agents used as general hemostatics act in two ways: (1) coagulants of the blood; and (2) constrictors of the vessels.

Coagulants of the Blood.—These use the absorptive power of colloids of the blood to modify their molecular state and obtain direct coagulation.

Two classes exist, the mineral ions, as, for example, calcium chlorid, sodium sulphate, Rabel water, iron perchlorid, saline solution, and artificial sera; and substances which form complex insoluble colloids, for example, gelatin, serum, organic extracts, and peptone.

Mineral Ions.—While the author feels very dubious as to the efficacy of mineral salts in this disease, there are many with whom they have found favor. Of the mineral ions the calcium salts are used internally, or locally, or as an irrigation. Arthus was among the first to show the important part played by calcium salts, especially calcium chlorid, in blood coagulation. Wright, Carnot, and others used it for hemorrhage, and it was found that calcium chlorid in 1 per cent solution, applied locally to a wound, would stop the bleeding. Wright, too, showed that the same effect was produced when given by the mouth, the action taking place in a few hours after the first dose. From 2.0 to 4.0, or even 8.0 gm. are given daily, well diluted. The following mixture may be of use:

℞	Calcii chloridi	12.00 gm.	ʒiii
	Aquæ destillatæ	120.00 gm.	℥iv
	Syrup aurantii	120.0 gm.	℥iv

One dram of this mixture contains 1.0 gm. calcium chlorid, and this should be given three times daily. The same mixture has been used with success in hemophiliacs as a preventive when operations were necessary.

Calcium may be used in the form of limewater, ½ oz. three times a day in milk, or water will suffice. It may or may not be used in the form of the lactate, 5 gm. t.i.d. Calcium chlorid, which is used in the same dose, well diluted, may be given, though it is apt to irritate. It has no advantage over the other forms.

Many writers have cited the successful employment of this means of hemostasis both for preventive and curative purposes. Among others may be mentioned Clifford, Perry, Manuel Simpson, Bryant, Fussell, and Wallis. However, in spite of these successful cases one may say that calcium does not "cure" hemophilia, and the treatment must be indefinitely continued. The results, too, are inconstant and temporary. While, in some of the cases cited where the coagulability was diminished, the calcium chlorid may act *inversely,* and coagulation will diminish if the injection of the salt be continued for three or four days. For this reason one must intermit the treatment every third day. Hypercalcification of the blood leads to diminished coagulability just as much as does decalcification. Boggs, Wright, and Paramore used calcium lactate in similar doses, finding it better tolerated and more efficacious. The English lay great stress on the efficacy of the calcium salts, while the Germans, as a class, are very dubious as to its benefits. Sahli and Nolf, for example, showed that it is absolutely useless in hemophilia, and, among the French authorities, Labbé proved its inefficacy in cases of purpura, for which it was used, and that the coagulation was unaffected. The work of Addis leads one to believe that the injection of calcium lactate in medicinal doses increases the quantity of calcium in the blood, but in proportions too small to increase in any appreciable way the time of coagulation.

Of the *artificial sera,* the injection of calcium chlorid solution and isotonic sea water has "cured" isolated cases, but whether this was a coincidence or an actual cure is not easy to say. Pelissard and Bonharnou record a case in a child a few days old, suffering from hemophilia neonatorum, thus cured after other styptics had failed, where, after 10 c.c. of sea water was injected, the hemorrhage ceased in two and one-half hours. Van der Velden employed in these cases:

Sodium chlorid, 5.0 gm.
Sodium bromid, 3.0 gm.

given daily by the mouth.

Reverdin, on the other hand, recommended 0.10 gm. sodium sulphate by mouth every hour.

Substances Which Form Complex Insoluble Colloids.—Gelatin was first administered as a coagulant by Dastre and Floresco. The gelatin was mixed with blood in vitro and the experiment showed that coagulation was favored, soft clots, such as are produced in normal blood, being formed. The gelatin is used in four different ways:

1. Locally, over a bleeding wound.

2. By mouth, 200 to 250 c.c. per day. It is doubtful if this method is useful, because the gelatin is changed in the alimentary canal to a non-hemostatic form.

3. Subcutaneously, 1 to 5 c.c. are mixed with sodium chlorid 0.7 gm., and distilled water 11 c.c.; this is sterilized by heat and used for injection. Twenty to 100 c.c. are daily employed.

Rénard succeeded with rabbits by subcutaneous injection and found, in 11 animals experimented on, that the coagulability was distinctly increased if large enough doses were used, that is, 0.2 gm. per kilo body weight. He found that the gelatin increased the fibrin ferment. Toussaint, Heymann, and also Babinsky obtained success by this method, though Carnot found his results uncertain; Labbé and Froin found no hemostatic action whatsoever in various forms of hemorrhage (typhoid, tuberculosis, renal, and purpura). They studied the coagulation of the blood before and after the use of the gelatin and found no change. They likewise experimented on healthy rabbits, the results being again negative. Add to this the experiments of Gley and Camus, who found that the gelatin injected subcutaneously was, after all, not even absorbed, and, finally, the experiments of Gley and Richaud, who attributed any coagulating properties, if they existed, not to the gelatin but to the salts contained in it, and the value of the treatment seems to lose much of its certainty. Nolf and Herry attributed any action to the foreign albumin, which excites the formation of thrombozyme secreted by the vascular endothelium and the leukocytes. It would seem, then, that *gelatin injections given subcutaneously are of little value,* because uncertain, slowly absorbed, painful, and liable to cause fever and sometimes even tetanus.

4. Intravenously, Salomoni found the injection of gelatin into the veins of great success where it is borne in large quantities, but without producing coagula in the vessels. It disappears slowly. Blood thus injected coagulates more rapidly than normal blood, but the clot is soft, not permanent, and retractile. He, too, found the subcutaneous method unsatisfactory, because gelatin is absorbed very slowly and then only by the lymphatics.

Serum Therapy.—Serum therapy differs from treatment by transfusion or from injection by defibrinated blood. The objects are preventive, curative, and stimulating to the marrow. Among the first to use serum therapy for hemophilia was Bienwald, who employed it for intractable hemorrhage from the scalp in 1897, using the grandmother's blood locally for the child. A cure resulted. Perthes followed in 1905. Fry, in 1898, successfully treated 3 cases of hereditary hemophilia by subcutaneous injections of horse serum, using 90 to 300 c.c. at an injection. Discos and Giroud stopped 6 cases of hemorrhage by using an antidiphtheritic serum,

and Welch, in 12 cases of hemophilia neonatorum, got successful results with human serum, when previously 17 out of 18 cases treated with calcium, gelatin, adrenalin, etc., had died. Ten c.c. of normal human blood-serum was used three times a day for the first day, and once on each subsequent day. The same success was attained by Bigelow in 3 cases of hemophilia neonatorum; 5 c.c. of fresh rabbit serum was given subcutaneously with immediate arrest of the hemorrhage.

Weil has perhaps done the best work in connection with this form of treatment. In one patient with severe attacks of spontaneous bleeding since infancy, with intervals between the hemorrhages of not more than three months, treatment during an attack of hematuria resulted in immediate cessation of spontaneous bleeding, while even after cuts into the skin no excessive bleeding occurred. As the intervals between the injections lengthened, however, recurrences took place, but the coagulation time was shortened from four and one-half hours to forty minutes. The same course of events took place with other hemophiliacs in the same family.

Weil recognizes two types, the one, sporadic hemophilia—that is, accidental with no hereditary tendency, where the blood has no coagulative ferment. In these cases he found that the injection of fresh serum intravenously completely cures the hemorrhagic tendency, and coagulation occurs in the normal time, five minutes, instead of one and one-quarter hours or longer. One can do operations after the injection, such as the removal of teeth, incision for empyema, etc., and this salutary condition persists for five weeks, after which the serum must be renewed and will produce the same good results. In the other, the hereditary form, the treatment is less effectual, coagulation is merely somewhat accelerated, and the hemorrhagic tendency is reduced. The results, however, are inconstant and merely temporary, for the serum is eliminated in four or five weeks, as is shown by the precipitin test (Marfan and Lemair).

The Kind of Serum to Be Used.—The object of this treatment is to supply to the blood the element that was lacking to cause coagulation. One must therefore use fresh serum, that is, less than two weeks old. Human serum or that from the horse or rabbit is best. Leary advises rabbit serum. He aspirates under asepsis, from the left ventricle of the heart, and recommends this for subcutaneous use. One may also use antidiphtheritic serum as being equally efficacious, but beef serum is bad, producing, as it often does, fever, cyanosis, and other signs perhaps attributable to anaphylaxis.

Intravenous Administration.—This is the best method, because most rapid and efficacious. Ten to 20 c.c. of the serum are injected and repeated in four weeks. Some authorities recommend that intravenous injections should be limited only to extreme cases, and then that the human serum alone should be employed. Twenty cases of Leary's so treated were

most successful, and toxic symptoms (urticaria) were present only in one case; in most instances only one injection was required.

Subcutaneous Administration Method.—This is less rapid but simpler. Twenty to 40 c.c. are used. Walters and Eaton used horse serum and diphtheria serum every two months hypodermically in doses of 20 c.c. with good results. Jennings reports cure of the hemophilic state in an infant of four days by two injections of normal horse serum, 8 and 7 c.c. respectively, given at nine-hour intervals. Similarly Clough controlled the situation in a hemophilic girl of fourteen in whom ergot, stypticin, calcium chlorid and gelatin had been given without result. Thirty c.c. of horse serum was injected, and three months later treatment was continued by injections of the mother's blood repeated at three-month intervals. Traver reports immediate results from the subcutaneous injections of human blood-serum in a boy of five who bled for six days from a slight cut on the tongue. The blood from his father was placed in the ice-box for ten hours, and 20 c.c. of the serum thus obtained was injected subcutaneously into the buttock. Immediate clotting (within twenty seconds) took place over the wound. The injection was repeated twice at eight-hour intervals. Successful series of cases are also reported by Nicholson, Reuben and others.

Local Applications.—The local application of serum by plugging, by compress, etc., may be combined usefully with injections and often assists the arrest of hemorrhage.

Transfusion (*See Pernicious Anemia for details*).—This method is of comparatively recent date for the treatment of hemophilia, and is by far the most satisfactory of all methods. Blood-platelets are thereby supplied in addition to the other constituents of the blood.

Direct Method.—The *direct* method of transfusing whole blood is undoubtedly more satisfactory in hemophilia than the use of the citrate method. Bulger's experience seemed to indicate but little change in coagulation time after the use of the citrate method. Vincent used direct transfusion in 11 cases and cured 8. Ottenberg and Libman treated 5 cases successfully, and suggest that every hemophiliac should have donors ready whose blood is known to be compatible.

One must not, however, expect permanent results from one transfusion, the probable reason being, as suggested by Minot and Lee, that the life duration of the platelets is a matter of days only; hence the improved coagulation time of the blood is limited to days. They recommend the use of large quantities to produce a longer effect. This is of especial use as a prophylactic for hemophiliacs who are obliged to undergo minor operations. A second transfusion is often necessary to insure the persistence of the normal coagulation time during the danger period following operation.

Organic Extracts (*Thyroid, Ovary, Liver, Etc.*).—These agents doubtless belong rather to the vasoconstrictors and their action is merely tran-

sient. On the theory that prothrombin is deficient in hemophilia, one may attempt to treat by adjusting the prothrombin-antithrombin balance by introducing thrombin or prothrombin into the circulation or by stimulating the tissues to produce more thrombin, or again by neutralizing relative excess of antithrombin by injecting tissue extracts. Brain lipoid has been found to be a useful source of fibrin ferment and a diphosphate, *Kephalin,* present in brain tissues and extracted with ether, has been used in hemorrhagic diseases, and is most efficacious as a local hemostatic. Its action on normal animals is to cause temporary coagulation, while in hemophiliacs the action is more permanent. Hurwitz and Lucas commended its use especially as a local hemostatic in capillary oozings. *Thyroid* was used by Dejage, by Combemale, and Gaudier with success, and spontaneous hemorrhages, which other methods had failed to prevent, were stopped. But these were in cases of purpura, not hemophilias. Scheffler claims to have stopped epistaxis in morbus maculosis Werlhofii by capsules of thyroid extract, and Royd Jones likewise. Faller speaks of cure of hereditary hemophilia in an infant which was cachectic from cutaneous and renal hemorrhages coming on after a second dose of extract of thyroid gland. *Ovarian* extract has been successfully tried by Lavadier in obstetrics, and *hepatic* extract has been shown by Gilbert and Carnot, by Foa and Pellacani, and also by Heidenhain to accelerate coagulation in vitro. All organic extracts have the same properties (Wooldridge Contajean), that is, they sometimes cause coagulation, sometimes anticoagulation; those most active are derived from the spleen, kidney, and pancreas. While useful in hemorrhagic states other than hemophilia, organotherapy may be said to be useless in the hereditary malady.

Coagulose (P. D. and Co.).—Coagulose, an anhydrous powder, sterile and soluble, containing fibrin ferment for clotting blood, is now much in vogue. It is supplied in bulbs; contents of one bulb are dissolved in from 6 to 8 c.c. of sterile water, well shaken, and injected (Collander). Tallant records successful use of the drug.

Peptones.—Nolf injected propeptone (Witte's) for hemophilia and found that rapid injection intravenously made the blood incoagulable, but when slowly inserted, or when used subcutaneously, it provoked an abundant secretion of thrombozymes and increased coagulability. The following is used:

> Peptone (Witte), 5.
> Solution Sodii chlor., ½ per cent, 100.

Sterilize by heat for fifteen minutes at 120° F. and inject subcutaneously from 10 to 20 c.c. This can be often repeated without any danger of anaphylaxis as a rule, though sometimes rather severe symptoms supervene, with the onset of fever, chills, nausea, headache, and general erythema, especially when the larger doses are given. Nolf and Herry regard

this treatment as better than the serum method, and Nobecourt and Tixier cured a case of hereditary hemophilia by this means where the serum treatment had failed. They used the subcutaneous method, injecting 38 c.c. of a 5 per cent solution, giving seven injections in the course of two and one-half months. Their experience, in this case, leads them to believe that rectal injections are quite as good as those which are subcutaneous.

Vasoconstrictors.—These are ergot, rathania, adrenalin, pituitary extract, tannin, stypticin, hydrastis canadensis, hamamelis virginica.

Ergot of Rye.—The powder is used, 2.0 to 6.0 gm. daily, in cachets, or by infusion. Or the extract of ergotin is used 1.0 to 4.0 gm. in pills or liquid. For hypodermic use Ergotin Yvon is recommended, 1 to 4 c.c. Ergotinin, that is, the alkaloidal extract of ergot (Tanret), is also used hypodermically, ½ to 2 mg. daily. By itself, ergot is useless, though it helps perhaps the action of other coagulants.

Rathania.—This is even less useful than is the ergot; it is liquid, and the extract is used in doses of 1.0 to 5.0 gm. daily.

Adrenalin.—This is used sometimes locally for a bleeding wound, as, for example, after adenoid vegetations or where the gums are bleeding. Sahli thinks that small hemorrhages result from its use, and maintains that the subcutaneous injections are dangerous. Whether or not this is an exaggeration it is difficult to say, but experience teaches that the indiscriminate use of adrenalin is both dangerous and productive of very serious results. It is certainly contra-indicated in chronic nephritis and aortic disease. In purpuras Labbé succeeded with doses of 0.0005 gm. subcutaneously, as did also Renon and Fenwick.

Cholesterin in Paroxysmal Hemoglobinuria.—Meyerstein showed rabbits which had been saturated with cholesterin remained without reaction after intravenous injections of soap solution, while in the control rabbits (not treated with cholesterin) soap solution produced hemoglobinemia and hemoglobinuria. Kurz and Grimm cured several cases of black water fever which had run their course under the form of a cyclic recurrent hemoglobinuria by the internal administration of cholesterin. On the ground of such observations, and because of the known action of cholesterin in stopping the hemolytic process in vitro, Pringsheim treated a case of paroxysmal hemoglobinuria under his care by daily intramuscular injections of 0.5 gm. cholesterin in 10 per cent emulsion of physiological salt solution. The attack was frustrated, the chill and fever occurring, but no blood appearing in the urine; after stopping the injections the sensibility to cold returned. An explanation of the action of the cholesterin upon these cases is not attempted, but the conclusion lies near that the same process is at work in vivo, in the arrest of hemolysis, as occurs when cholesterin is added in vitro.

Radium.—The action of radio-active substances upon the cellular contents of the blood, and their therapeutic possibilities in this connection, have been mentioned under Anemia and Leukemia. The further effect upon the body ferments was one of their earliest biological properties to be known, and has been made the subject of extensive studies by Lowenthal, Bickel, Weil, Wohlgemuth and others. Thus Lowenthal and Wohlgemuth found it accelerated the action of the diastatic ferment in the blood, bile, saliva, and pancreatic juice in a large number of cases, the acceleration being preceded by a temporary inhibition. In some cases only the inhibitory action was apparent, the variation probably resulting from a variation in the strength of the emanation, or in the concentration of the ferment solution. These observations were applied by Van der Velden to the problem of shortening the coagulation time of the blood, on which he found that radium, like peptone and other bodies, has definite effect. It has been established by him by experiments, both in vitro and in vivo, as well as by clinical observations, both in the normal subjects and in two cases of hemophilia studied, that radium emanations, whether given by the mouth or by inhalation, shorten the coagulation time to an appreciable extent. The effect is transitory, passing off with the emanations. The mode of action is not by any means understood, for the combination in which the emanations exist in the blood is not itself established. It may act directly by replacing or assisting the activating principle, thrombokinase, or (following the chemical theory of coagulation) by acting as thromboplastic substances do, by hastening the reaction, or indirectly by causing the passage of lymph from the adjacent tissues into the blood-stream by reason of the sudden physical or chemical changes induced. In any case the observation that radium shortens the coagulation time of the blood is definitely established, and in the further development of our knowledge of radio-activity, this fact may be found to have a definite bearing on the treatment of the hemophilic state. Neuffer seems to have obtained at least temporary benefit from irradiation of the spleen, due, he thought, to the liberation of thrombokinase.

Local Treatment.—Local treatment in hemophilia is, of course, useful mainly for wounds. Compression and ligature of vessels, however, seem to be useless. The compresses of Anadon and Pengewar are useless for hemophilia, as are also antipyrin, stypticin, and perchlorid of iron, which, although useful in hemorrhages of healthy people, are utterly ineffectual in hemophilia. Calcium chlorid and gelatin likewise are of very little use when applied locally in this condition.

The best general treatment, namely, the application of serum or organic extracts, is also the best local treatment. Fresh serum saturating the lint and applied to a wound is all-powerful, and may also be used as a plug for the nostrils or for bleeding teeth. Serum has likewise been used with excellent results as a dry powder. Nolf prefers the organic

extracts of the lymphoid organs, especially the spleen, the glands, and the thymus, and uses these in the fresh state pulverized. Schloessmann advocates the local use of sterilized tissue extracts, such as may be obtained from parenchymatous hyperplastic goiter, and considers these to be at once the most harmless and the most useful local hemostatic known. The organ is first triturated with a little fine sand (washed and sterilized); this is boiled and sterilized and salt solution added (0.9 per cent sodium chlorid and 0.5 per 1,000 calcium chlorid). Two pounds of the solution are used for 1 pound of the organ. The liquid is applied sterilized, soaked with cotton wool and used for a few minutes, or hours, as the occasion requires.

Sayer used his own blood, obtained by cutting his finger, locally to a wound on a hemophilic boy's forehead, which instantly stopped bleeding. Bluhdorn used with success fresh sterile human serum on a tampon to the wound, as well as injections at its border, in a case of melena and purpura with hemorrhage from the cord in pernicious jaundice of infancy.

Treatment of the Hereditary Form.—Two considerations must be taken into account. First, the treatment from the onset of the first symptom, and, secondly, the treatment during the remissions.

Victims of this disease must be treated soon, and the treatment continued for a long period. One should start either with serum or with peptone, and the agent used should be repeated in four weeks. No anaphylaxis results, and it is well in every case to follow the practice of Netter, who gives at the same time 2 to 4 gm. daily of calcium chlorid. It is well to examine for the coagulation time systematically, in order to direct the treatment properly. This applies equally for the serum treatment and for the peptone treatment.

In hemophiliacs in successive stages, with remissions of variable duration, one need not continue the serum treatment during the remissions, but recommence at the earliest sign of renewed symptoms, as, for example, the outbreak of petechiæ. Excellent results are shown in numberless cases that have already been reported. Thus, for example, one of Weil's cases, who bled for twelve hours whenever he cut himself shaving, bled for only two minutes after a serum injection; and the same patient, who was subject to hemarthrosis once a month, was freed from symptoms for eleven months. In another instance the hematuria, which had lasted one month, definitely stopped on the third day after the injection.

Local treatment by serum is also given; and 1 c.c. of the defibrinated blood of the rabbit injected locally will stop oozing from the gums which may have lasted previously for weeks.

Treatment of Sporadic Cases.—This is a less severe illness and liable to subside as life goes on, so that, after recoveries from attacks, there is less need of interval treatment. Otherwise the therapeutics are the same as in the hereditary types.

In hemophilic states of secondary or associated types, as, for example, in pernicious anemia, etc., the condition is analogous to that in true hemophilia, though not identical, that is, there are hemorrhage, plasmatic coagulation, retarded coagulation, absence of clot retraction, and absence of exudation of serum. All these anomalies decrease in vitro when small amounts of fresh serum or calcium chlorid are added. The same treatment is given as in the other hemophilias. That is to say, for example, if in pernicious anemia petechiæ or hemorrhages with diminished coagulability develop, the serum or peptone treatment should be added to the regular treatment of the underlying condition. Vasoconstrictors, however, should only be used if the hemorrhage is very severe. The same refers to the purpuras, though Labbé did not have the same success here with the serum treatment as did Weil. The coagulability was improved, but the hemorrhages continued as though the serum acted on the hemophilic state without acting on the purpuric. Nobecourt and Tixier found peptones very useful in purpura as well as in hemorrhages from the liver, the kidneys, or those occurring in infective diseases and toxic states.

During the remissions organotherapy should be used first, for two weeks every two months. By this is meant the injection of hepatic or splenic extract, which may help to maintain a reasonable degree of coagulability and keep off a return of accidents.

Vasoconstrictors should be given alternating with opotherapy, that is, for two weeks every two months, to maintain the tonicity of the vascular muscles. Thus, for example:

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Tr. hamamelis virginica, 1.0 to 4.0 gm. daily.
Or fluid extract virginica, 1.0 to 20.0 gm.
Or dry extract virginica, 0.10 to 0.20 gm.

daily in pills. Or, again,

Hydrastis canadensis as the tincture, 20.0 to 30.0 c.c.
Or fluid extract canadensis, 1.0 to 4.0 c.c.
Or hydrastin, 0.02 to 0.03 gm. in pills.

This is of use chiefly in uterine hemorrhages.

Ergotin, 0.5 to 1.0 gm., may be also used daily in pills.

Strychnin in various forms has also been recommended.

Nux vomica as a powder, 0.05 to 0.1 gm. daily, or the tincture, 15 to 20 drops daily, or, again,

Sulphate of strychnin, 1 to 2 mg. in pills, may be recommended.

During all this time the diet should be nourishing in order to regenerate the red cells and hemoglobin, and the yolks of eggs and rare meats are especially efficacious. Vegetarian diet is not to be recommended.

Treatment of Accidents and Hemorrhages.—In addition to general dietetic treatment, one is often called upon to use special therapeutic

agents for the accidents in this disease. In the first place, prophylactically speaking, one should avoid carefully all chances of injury when epistaxis tends to occur; the part should be plugged at once with tampons soaked in serum or extract of spleen; and after teeth extraction an alveolar hemorrhage should be treated locally by plugging in a similar fashion, a ball of cotton being soaked in the serum and gripped between the teeth for half an hour. Superficial oozing of the skin should be treated with compresses of serum or splenic extract. For the intestinal and gastric hemorrhages the patient should be made to swallow fresh serum or powdered liver or spleen extract diluted in artificial serum. Or one may try gelatin serum, or a 0.2 per cent solution of calcium chlorid. Renal and pulmonary hemorrhages are not accessible to local treatment and require rest, coagulants, and vasoconstrictors. Howell suggests testing all bloods prior to any operation on patients exhibiting a hemophilic tendency. The blood is first oxalated and then recalcified with an optimum amount of calcium.

If all these fail one can then resort to the hypodermic injection of adrenalin, ½ to 1 mg. at a dose. Curiously enough, some authorities advise the use of vasodilators in these conditions, such as amyl nitrate inhalations, but the practice has been shown to be dangerous. For the posthemorrhagic collapse, caffein, oil of camphor, ether, strychnin, and strophanthus may all be used.

Arthropathies.—These are among the most distressing symptoms, and, apart from the general treatment as given above, the joint should be immobilized and covered over with protecting bandages and soothing lotions. For the pain, salicylates or morphin should be used. Later on, the joint should be fixed in order to avoid the recurrence of hemorrhages.

Anemias.—These should be treated by a subcutaneous saline at the time of acute hemorrhage in order to restore the mass of fluid; and arsenical preparations may be given with the hope of stimulating the bone marrow functions, or iron may be given with the hope of restoring the hemoglobin.

REFERENCES

General Articles

Arnsperger. Treatment of Hemorrhagic Diathesis, Deutsche med. Wchnschr. Synopsis in Arch. d. mal. du cœur, January, 1911.

Howell. The Condition of the Blood in Hemophilia and Purpura, Arch. Int. Med., No. 13, 1914.

Hurwitz and Lucas. A Study of the Blood in Hemophilia, Ibid., 543, April, 1916.

Labbé. L'Hémophilie, Pathogénie et Traitement, Journ. Méd. Franc., 1910.

Litten, M. Art. Hemorrhagic Diseases, Nothnagel's System, edited by Stengel, 1905.

Lucas, Wm. Palmer. Bost. Med. & Surg. Journ., November 18, 1909.

Matthews and Carpenter. Purpura Hæmorrhagica, with Report of an Atypical Case, Am. Journ. Med. Sc., July, 1911.

Ranzier. Modern Treatment of Hemorrhages, Synop., Arch. mal du cœur, September, 1910.

Sahli. Uber des Wesen der Hämophilie, Ztschr. f. klin. Med., lvi, 264, 1905.

Weil, P. E. Étude du Sang chez les Hémophiles, Bull. et Mém. Soc. méd. d. Hôp. de Par., October 26, 1906.

——— Recherches Cliniques et Pathologiques sur l'Hémophile d'après Sixcas, Bull. et Mém. Soc. méd. d. Hôp. de Par., November 2, 1906.

——— La Coagulation du Sang dans les États Hémorrhagiques, Compt.-rend. Soc. de biol., December 8, 1906.

Wright, Sir A. E. Hemophilia, Allbutt and Rolleston's System, v, 918-946, 1909.

Calcium

Addis. Effects of Administration of Salts of Calcium (lactate), and Citric Acid on Blood Content of Calcium and on Time of Coagulation, Quart. Journ. Med., Jan., 1908.

Lambert. Calcium Chlorid in Hemorrhage, Brit. Med. Journ., July 13, 1907.

Wright. Effect of Administration of Calcium Salts in Hemorrhage, and in Actual and Threatened Hemorrhage, Ibid., ii, 223, 1893.

Gelatin

Renar. Contribution to Study of Influence Exerted on Coagulability of the Blood by Gelatin. Synop., Arch. d. mal dur cœur, February, 1911.

Salomoni. Value of Gelatin as an Hemostatic Agent, Riforma med., 172, 254, 1900.

Artificial Serum

Pelissard and Bonharnon. Injections of Isotonic Sea Water (plasma de Quinton) in Hæmophilia Neonatorum, Presse méd., 77, 1906; Synop., Folia hæmatol., i, 278, 1907.

Serum Therapy

Bigelow. Serum Treatment of Hemorrhagic Disease of the Newborn, Journ. Am. Med. Ass., July 30, 1910.

Bluhdorn. Uncontrollable Hemorrhages in Infancy, Berl. klin. Wchnschr., No. 50, 11, 1913.

Clough. Hemophilia Treated by Repeated Injections of Blood Serum, Journ. Am. Med. Ass., July 12, 1913.

Discou and Giroud. Treatment of Hemorrhage by Antidiphtheritic Serum, Loire méd., Sept. 15, 1909.

Elser and Meader. Chronic Purpura, and Its Treatment with Animal Serum, Am. Journ. Med. Sc., 178, Feb., 1913.

Fry. The Successful Treatment of Hemophilia by the Injections of Serum, N. Y. Acad. Med., June 2, 1898.

Gangani. On the Use of Serum as a Hemostatic in the Hemorrhage of Hemophilies. Synop. Folio hæmatol., April, 1910.

Giroud and Laurent. Traitement des Hemorrhagies Rebelles par les Injections de Sérum Antidiphtherique, Thèse de Lyon, 1909.

Jennings. Horse Serum in Hemorrhagic Disease of the Newborn, Journ. Am. Med. Ass., April 12, 1913.

Leary. Use of Fresh Animal Sera in Hemorrhagic Conditions, Bost. Med. & Surg. Journ., July 16, 1908.

Lommel. On Arrest of Hemorrhage in Hemophilia by Serum, Zentralbl. f. innere Med., 27, 28, 1908.

Nicholson. Therap. Gaz., Feb., 1912.

Reuben. Defibrinated Blood in Hemophilia, München med. Wchnschr., Oct. 1, 1912.

Roussot. Hemostase par le Sérum Sanguin, La Methode de P. E. Weil en Chirurgie, Thèse de Lyon, 1910, 47, 1909-1910.

Sayer. Journ. Am. Med. Ass., Jan. 13, 1913.

Schwartz and Ottenburg. Hemorrhagic Disease of Newborn, with Especial Reference to Serum Therapy and Coagulation, Am. Journ. Med. Sc., July, 1910.

Schleuker. Journ. Am. Med. Ass., 1916.

Traver. Ibid., Jan. 4, 1912.

Wallace. Accidents with Antidiphtheritic Serum, Med. Rec., Jan. 7, 1911.

Welch, J. E. Normal Human Blood Serum as Curative in Hæmophilia Neonatorum, Am. Journ. Med. Sc., June, 1910.

Weil, P. E. L'Hemophilie, Pathogénie et Serotherapie, Presse méd., Oct. 18, 1905.

——— Des Injections de Sérums Sanguins Frais dans les États Hemorragipares, Tribune méd., Jan. 12, 1907.

——— Traitement de l'Hemophilie par les Injections de Sérums Sanguins Frais, Cong. Franc. de méd., IXième Session, 1908.

——— Action of Injections of Fresh Blood Serum in Blood States That Give Rise to Hemorrhage, Internat. Clin., xvii, 1907.

——— Serum Therapy of Hemorrhagic Purpura, Tribune méd., 1907.

Wilson. Med. Rec., Aug. 10, 1912.

Transfusion of Blood

Coca. Cause of Sudden Death after Intravenous Injections of Heterogeneous Blood, Univ. Penn. Med. Bull., Oct., 1908.
Dorrance and Nate. Vein to Vein Transfusion of Blood, Journ. Am. Med. Ass., Aug. 13, 1910.
Duke. Relation of Blood Platelets to Hemorrhagic Disease, Ibid., Oct. 1, 1910.
Hahn. Hemophilia Treated by Transfusion, Med. Rec., October 8, 1910.
Hotz. On Transfusion of Blood in Man for Hemorrhage, Ztschr. f. Chir., civ, April, 1910.
Mosenthal. Transfusion as a Method of Treatment of Hæmophilia Neonatorum, Journ. Am. Med. Ass., i, 1910, 1913.
Ottenberg and Libman. Am. Journ. Med. Sc., i, 1915, 1912.
Pepper and Nisbett. A Case of Fatal Hemolysis Following Direct Transfusion of Blood by Arteriovenous Anastomosis, Journ. Am. Med. Ass., xlix, 385, 1907.
Schelbe. Treatment of Infantile Anemia by Transfusion of Blood, Jahrb. f. Kinderh., Oct., 1908.
Schloss and Comminskey. Am. Journ. Dis. Child., April, 1913.
Vincent. Transfusion in Hemorrhagic Disease of Newborn, Arch. Pediat., No. 29, 887, 1912.

Transfusion of Whole Blood

Bulger. Journ. Lab. & Clin. Med., vi, 1920.
Emsheimer. Journ. Am. Med. Ass., 1916.
Fonio. Cor.-Bf. f. schweiz. Aerzte, xlv, 1915.
Howard. Kentucky Med. Journ., 1914.
Jarvis. Bost. Med. & Surg. Journ., April, 1914.
Minot and Lee. Arch. Int. Med., xviii, 1916.

Coagulen

Frank. Berl. klin. Wchnschr., 1915.
Halpen. Beitr. z. klin. Chir., 1915.

Coagulose

Collander. Therap. Gaz., xxxviii, 1914.
Tallant. Women's Med. Journ., Dec., 1915.

Peptones

Martz. Abstract, Schmidtzjahrb., Sept., 1913.
Nolf and Herry. Pathogenesis and Treatment of Hemophilia, Rev. de Méd., 12, 1909; 1, 2, 1910.
Nobecourt and Tixier. Bull. et Mém. Soc. méd. d. Hôp. de Par., Oct. 22, 1910.

Radium

Neusser. München. med. Wchnschr., lxviii, 1921.

CHAPTER XXXIX

CHRONIC HEMOLYTIC JAUNDICE

WILDER TILESTON

Synonyms.—Chronic acholuric jaundice, chronic familial jaundice or cholemia, hemolytic splenomegaly, hemolytic anemia.

Definition.—A condition in which there is chronic jaundice with bile pigment in the stools but none in the urine, usually accompanied by anemia and enlargement of the spleen, and by diminished resistance of the red cells. Two forms are observed, the hereditary and the acquired.

History.—The first accurate description of the hereditary type was published by Minkowski in 1900. Chauffard in 1907 made the important discovery that the resistance of the red cells to hypotonic salt solutions was markedly decreased, and a year later reported the presence of numerous reticulated red cells. The acquired type was first described by Hayem in 1898, and more fully in 1907 by Widal, who was the first to recognize its hemolytic nature. For these reasons the expressions "Minkowski-Chauffard," and "Hayem-Widal" are sometimes used to designate the two types of the disease.

THE HEREDITARY TYPE

The hereditary form, often wrongly called "congenital," belongs to the interesting group of inheritable diseases, occurring often in several generations. The condition is probably inherited as a dominant Mendelian character, according to Meulengracht. This is indicated by the facts that approximately one-half of the children are affected, and the descendants of unaffected members of a family always remain free from the disease. The first case in a given family is assumed to arise by mutation.

Etiology.—The etiology is obscure. Syphilis and tuberculosis have been incriminated, but these diseases are absent in most cases. The sexes are involved with equal frequency, and there is no racial predisposition.

Pathology.—The spleen is often greatly enlarged, weights of 1,000 gm. and over being not unusual. The capsule may be thickened and

adherent, but the trabeculæ and follicles are essentially normal. The most striking feature is the marked engorgement, which on microscopical examination is found to have an unusual distribution, the pulp being crowded with red cells, while the sinuses are nearly empty. There is a variable amount of pigmentation, often very marked, and chiefly within the endothelial cells lining the sinuses; it usually gives the iron reaction. The liver, as a rule, is not enlarged. There are no signs of cirrhosis, nor of obstruction of the bile ducts, unless there is a complication with stones in the common duct. The parenchymal cells are normal except for deposition of pigment similar to that in the spleen. Gall-stones are present in about 60 per cent of the cases. The bone marrow of the long bones is red and in a state of great activity. The lymph-nodes may be pigmented and may be the seat of hemolysis. A marked siderosis of the kidneys has been found in a few instances.

Pathogenesis.—That the jaundice is hemolytic in character is shown by the marked increase in the urobilin excretion, found by Eppinger and others; by the pigmentation of the organs of hemolysis, the splenomegaly, and the absence of signs of obstruction of the bile passages.

The important researches of Hijmans van den Bergh have shown that two varieties of bilirubin may be found in the blood in jaundice; one which gives the "prompt direct" reaction with Ehrlich's diazo reagent is found only in obstructive jaundice; the other, giving a delayed or negative direct reaction, but demonstrable after treatment of the serum with alcohol, is found in hemolytic jaundice, and also in small amounts in normal blood. The former variety is excreted by the kidneys after a certain threshold is exceeded; the latter, met with in hemolytic jaundice, is incapable of excretion, but urobilin appears in the urine in its place.

There is considerable evidence that bile pigment of this second variety is formed in the "reticulo-endothelial system" of Aschoff, which includes the endothelial cells of the spleen, liver, bone marrow and lymph-nodes, and is probably absorbed from the portal capillaries by the liver cells and secreted into the bile capillaries, being altered in its passage so that it now gives the "prompt direct" reaction of ordinary bile. For a clear exposition of the newer views on jaundice, the reader should consult the critical review by McNee.

The facts upon which a theory of pathogenesis must depend are as follows: There is an increased fragility of the red cells as shown by testing with hypotonic salt solutions. The jaundice and the anemia are the results of excessive hemolysis, which takes place chiefly in the spleen. After splenectomy a clinical cure is observed, but the diminished resistance of the red cells persists. It is therefore unlikely that increased hemolysis by the spleen is the true cause of the disease, which must rather be sought in a constitutional anomaly of the bone marrow, resulting in the formation of abnormally fragile red cells.

Symptomatology.—The patient, as a rule, experiences little inconvenience from his disease, and as Chauffard has remarked, is jaundiced rather than sick. Epistaxis is common during adolescence, but hemorrhages from other sources are not encountered. From time to time attacks occur, the so-called "crises of deglobulization" of the French, in which there are fever and increased jaundice, sometimes pains over the liver and spleen, and a rapid fall in the red cell count, with a still further lowering of the resistance of the red cells. It has been noted that, although the older members of the family are robust, succeeding generations are apt to show signs of constitutional inferiority, such as weakness, delayed puberty or infantilism, prognathia, steeple skull or club-foot, as noted by Mayer, Curschmann and others. In the more severe cases the frequent crises and anemia may incapacitate the patient for work, and chronic persistent ulcers of the legs may develop.

Jaundice.—Jaundice may be present from birth, or appear in childhood or early youth, or exceptionally not until the third decade. It is usually slight or moderate in degree, and never assumes the greenish hue met with in some cases of obstructive jaundice. It is never accompanied by itching, bradycardia or xanthomata. It varies in intensity from time to time, increasing after fatigue, or exposure to cold, during pregnancy, and particularly at the time of crises. In a few otherwise typical cases jaundice has been permanently absent, and in the family described by Poynton there were recurrent attacks of icterus, while in the interim there were anemia and splenic tumor, but no jaundice.

Spleen.—The spleen is almost constantly enlarged to a degree roughly corresponding to the severity and duration of the disease. It may attain the dimensions of the leukemic spleen, but more commonly it reaches about to the umbilicus. In some cases the enlargement is slight or even absent. During the crises the organ becomes still further enlarged and may be painful.

Blood.—A moderate anemia is the rule, but during crises there may be a marked decrease of the red cells, counts as low as one million having been reported. The hemoglobin is proportionately reduced, so that the color index is about one. The average size of the red cells is decreased, and there are more or less anisocytosis and polychromatophilia, while poikilocytosis and stippling are unusual. Normoblasts are often present. Reticulation of the red cells, as shown by vital staining, is seen to a degree found in no other disease. From 10 to 20 per cent of the cells may show it, but in a few cases it is lacking. The leukocyte count is usually normal, though there is sometimes leukopenia. There may be a polynuclear leukocytosis at the time of crises, but this is not constant.

The most important feature is the decreased resistance of the red cells to various hemolytic substances, and particularly to hypotonic salt solutions. This has been noted in almost all of the reported cases, but

has been lacking in a few, as in those of Holland. Usually it is present at all times in a given case, but exceptionally only during crises. Beckmann was able to induce lowered resistance in two cases in which it was absent, by exposure of the spleen to sunlight, massage and the X-ray.

Usually both the minimum and the maximum resistance are decreased, hemolysis beginning at 0.7 per cent to 0.5 per cent, and being complete at about 0.4 per cent, the normal figures being 0.44 per cent and 0.30 per cent, respectively. The serum is high-colored, and contains bilirubin in considerable amounts, of the kind that gives the delayed or negative direct reaction of van den Bergh. Although often far exceeding the threshold value that obtains in obstructive jaundice, bilirubin does not appear in the urine, possibly because, as Blankenhorn has shown, this form is not dialyzable. Hemolysins have been found in the blood in a few instances, usually as isolysins, rarely as autolysins. The cholesterol of the blood is never increased, as it is in obstructive jaundice. The free cholesterol, which in the test-tube has an inhibitory effect on hemolysis, is usually normal, sometimes decreased.

Urine.—The urine is free from bile pigment and bile salts, except at the time of crises, when both may appear temporarily, though usually they are absent. In all but the mild cases, it contains a considerable amount of urobilin and urobilinogen.

The *feces* are always well colored, and contain an excess of urobilin, an indication of increased hemolysis.

Metabolism.—The digestion and absorption of fat are normal. The elimination of iron is increased. The excretion of uric acid is increased, likewise the uric acid of the blood. McKelvy and Rosenbloom have reported a considerable loss of cholesterol with the feces.

Complications.—Gall-stones are encountered with extraordinary frequency, occurring in about 60 per cent of the cases. This is probably owing to the altered character of the bile, which is very rich in pigment. Gout is occasionally associated, but probably without any causal relationship.

Diagnosis.—The diagnosis depends upon the presence of chronic acholuric jaundice dating from birth or an early age, and associated with anemia, enlargement of the spleen and diminished resistance of the red cells. In atypical cases any one of these features may be absent, and the diagnosis rests upon the clinical picture taken as a whole. The demonstration of increased urobilin excretion, and of increased bilirubin in the blood, of the sort giving the delayed reaction, are of considerable value, though both these phenomena are present in pernicious anemia. A careful history, and the examination of other members of the family, are of great assistance. Thus in one of Giffin's cases the mother showed decreased resistance, though otherwise healthy, and Rosenthal found in the

mother of his case a high value for bilirubin in the blood, though there were no other signs of the disease.

Differential Diagnosis.—In differential diagnosis, cirrhosis of the liver, Banti's disease and gall-stones are the diseases most likely to cause confusion. Cirrhosis of the liver is excluded by the non-obstructive character of the jaundice, and the absence of signs of portal obstruction, such as ascites and collateral circulation. The early stage of Banti's disease is ruled out by the presence of jaundice and the diminished resistance of the red cells; the late stage by the absence of signs of cirrhosis. Syphilis of the spleen may be eliminated on similar grounds. Gall-stones cause jaundice of the obstructive type, and give rise to moderate enlargement of the spleen, only when there is infection of the bile ducts. A complication of hemolytic icterus by gall-stones may be suspected when attacks of biliary colic occur, though pain over the liver is sometimes felt during crises, apparently in the absence of gall-stones.

Gaucher's disease, or large-cell splenomegaly, is a very rare disease. It occurs in several members of a family, usually in females, and is never hereditary. Jaundice is lacking, the resistance of the red cells is not altered, and there is marked enlargement of the liver as well as of the spleen.

Cases occurring in infants might be confused with the diseases of this period which give rise to splenomegaly, anemia, or jaundice. The enlargement of the spleen of rickets, miliary tuberculosis and von Jaksch's disease is not accompanied by jaundice. Hereditary syphilis occasionally leads to icterus, usually of the obstructive type, and resort to a resistance test may be necessary, since a positive Wassermann reaction is sometimes encountered in hemolytic jaundice, owing to complication by syphilis. Familial icterus of the newborn is usually a rapidly fatal disease, and in those who recover the jaundice disappears permanently.

Prognosis.—The disease persists throughout life and is never fatal of itself, though the complicating gall-stones may prove serious.

Treatment

Medical Treatment.—In many cases no treatment is required. During crises the patient should be put to bed, and after the acute symptoms subside, should receive a nourishing diet with plenty of the iron-containing foods, such as meat, fish, eggs and spinach. Since blood regeneration is rapid after the crises, iron or arsenic given then will appear to be beneficial, but at other times these drugs have no effect on the anemia. Transfusion of blood has only a temporary effect, and cases severe enough to require it should have splenectomy done.

The administration of cholesterol is suggested by the fact that this substance inhibits hemolysis in the test-tube. Several French observers

have noted diminution of the jaundice with increase of the resistance of the red cells, but the effect was temporary, ceasing as soon as the drug was withdrawn. It may be given in doses of 0.2 to 1.0 gm. per day. Exposure of the spleen to the Roentgen ray may reduce the size of the organ somewhat, but it has no other good effect, and does not seem advisable.

In cases where hereditary syphilis is associated, specific therapy is indicated on general principles, but has no effect on the hemolytic jaundice.

Surgical Treatment.—The importance of the spleen in the process of hemolysis suggested its removal in hemolytic jaundice, which was first successfully performed by Micheli in 1911. Since that time splenectomy has been done a great many times, almost always with brilliant results. The jaundice disappears within a few days, the red count becomes normal, and the urobilin excretion drops, indicating a diminution of hemolysis. The decreased resistance of the red cells, however, usually persists, which shows that the underlying cause of the disease has not been removed. The cure, for it amounts to that, appears to be permanent; in Giffin's series all of the cases of the hereditary type were well at periods up to five years after operation. Occasional failures after splenectomy have been reported (Gerhardt).

The immediate mortality has been considerably reduced in recent years, Mayo reporting 19 operations with only 1 death. This is due partly to improved technic, partly to the practice of transfusing blood before the operation, and also afterwards if much blood has been lost. The indications for splenectomy are marked anemia, frequent crises, and great enlargement of the spleen. The complicating gall-stones often require surgical treatment, in which case the gall-bladder should be removed, as otherwise stones are likely to form again; this operation can be combined with splenectomy if the condition of the patient permits.

THE ACQUIRED TYPE

The acquired type is much rarer than the hereditary. It may be divided into two groups, cryptogenetic and secondary. In the former no cause can be assigned, while in the latter hemolytic jaundice occurs as a complication of some other disease.

Etiology.—The cause of the cryptogenetic form is obscure. In some cases the disease begins in connection with an infection of the intestinal tract, such as typhoid or dysentery, and persists after recovery from the infection, and it is possible that toxic substances are absorbed from the intestines, and stimulate in some way the hemolytic processes. In favor of such an origin may be cited the case of Widal, Abrami and Brulé (1912), in which hemolytic jaundice set in following ischiorectal abscess

with stricture of the rectum, and disappeared after the formation of an artificial anus, to reappear each time that the opening became obstructed. In a few cases the condition has followed excessive hemorrhage.

The secondary type has been reported in connection with syphilis, both hereditary and acquired, septicemia, malaria, pregnancy, cirrhosis of the liver, both biliary and portal, carcinoma and acute lymphatic leukemia.

Pathogenesis.—The pathogenesis in the cryptogenetic form is probably similar to that of the hereditary type. Two facts, however, seem to indicate that it is not identical with it: (1) the diminished resistance of the red cells usually disappears after splenectomy; (2) the disease is never transmitted to the offspring.

Pathology.—The pathology is the same as in the hereditary type.

Symptomatology.—The course differs in several respects from that of the hereditary type. It is usually more severe and often ends fatally. The anemia is more marked, the red count averaging two millions, while jaundice is often slight and may be lacking, in which case the term "hemolytic anemia" is more appropriate. The crises of deglobulization are more frequent and more intense. The resistance of the red cells is less diminished and in some cases normal; Widal found it normal with whole blood, but decreased with deplasmatized corpuscles.

Borderline cases are occasionally seen in which it is difficult to say whether one is dealing with pernicious anemia with diminished resistance, or a pernicious type of hemolytic jaundice. But the latter differs from pernicious anemia in the absence of involvement of the tongue and central nervous system.

Recurrent hemoglobinuria has been reported in a few instances by Giffin and others. This suggests a comparison with paroxysmal hemoglobinuria, from which it differs in the negative result of the Donath-Landsteiner test. (Slight hemoglobinuria occasionally occurs in the hereditary type, at the time of crises.)

Widal (1908) has described a phenomenon which he calls autoagglutination of the red cells, which is almost constantly absent in the hereditary type, and frequently present in the acquired. It consists in agglutination of the red cells into a dense pellicle, when mixed in a watch-glass with the patient's serum, in the proportion of 1:20.

Diagnosis.—The cryptogenetic form is recognized in the same way as the hereditary type. To differentiate between the two it may be necessary to examine the relatives, one of whom may have an unrecognized jaundice, or even decreased resistance without other signs of the disease. Increased fragility of the red cells is not a *sine qua non* for the diagnosis. Cases beginning after the third decade are almost certainly acquired. In general it may be stated that cases should be assumed to be hereditary until the contrary is proved.

The secondary form may be suspected when jaundice with splenomegaly develops in the course of one of the diseases mentioned above, if there is urobilin but no bile in the urine. The diagnosis is confirmed by finding diminished resistance, but may be made in the absence of this feature if the other signs are present, especially if the van den Bergh test shows bilirubin of the type giving the delayed reaction.

Prognosis.—The prognosis of the cryptogenetic form is not so good as in the hereditary type, since the disability is much greater, and there is a possibility of a fatal outcome. In the secondary form it depends in part on the nature of the associated disease.

Treatment.—The treatment is the same as in the hereditary type. Widal speaks warmly for the administration of iron. In the cases associated with syphilis, a cure may be brought about by specific treatment, which is not the case in the hereditary form. When the disease occurs in connection with pregnancy, termination of the pregnancy is indicated, and may result in recovery. Cases associated with malaria may be cured by quinin.

Splenectomy usually gives good results, provided that organic disease is absent, but failures are apparently more frequent than in the hereditary type. The presence of cirrhosis of the liver is not a contra-indication, but makes permanent improvement unlikely. In cases bordering on pernicious anemia splenectomy is justifiable, but the outlook is not so good, on account of the possibility of error in diagnosis.

REFERENCES[1]

Beckmann, K. Deutsches Arch. f. klin. Med., cxxx, 301, 1919.
Blankenhorn, M. A. Arch. Int. Med., xxvii, 131, 1921.
Chauffard, A. Semaine méd., xxvii, 25, 1907; xxviii, 49, 1908.
Curschmann, H. Ztschr. f. klin. Med., lxxxvii, 19, 1919.
Eppinger, H. Berl. klin. Wchnschr., l, 1509, 1572, 1913.
Gerhardt, D. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xxxi, 644, 1918.
Giffin, H. Z. Surg. Gynec. & Obst., xxv, 152, 1917.
——— Tr. Ass. Am. Physicians, xxxvii, 452, 1922.
Hayem, G. Presse méd., vi (Part I), 121, 1898.
Hijmans van den Bergh, A. A. Der Gallenfarbstoff in Blute, Leipzig, 1918.
Holland, M. Ztschr. f. klin. Med., lxxxvii, 72, 1919.
Mayer, K. Deutsche Ztschr. f. Chir., clxxi, 1, 1922.
Mayo, W. J. Med. Rec., xcii, 705, 1917.
McKelvy, J. P., and Rosenbloom, J. Biochem. Ztschr., lxviii, 78, 1915.
McNee, J. W. Quart. Journ. Med., xvi, 390, 1923.

[1] For additional references the reader is referred to a critical review by Tileston, Medicine, I, No. 2, 1922.

Meulengracht, E. Deutsches Arch. f. klin. Med., cxxxvi, 33, 1921.
Micheli, F. Wien. klin. Wchnschr., xxiv, 1269, 1911.
Minkowski, O. Verhandl. d. deutsch. Kong. f. innere Med., xviii, 316, 1900.
Poynton, F. J. Lancet, i, 153, 1910.
Rosenthal, F. Deutsches Arch. f. klin. Med., cxxxii, 129, 1920.
Tileston, W. Medicine, Baltimore, i, 355, 1922.
Widal, F., Abrami, P., and Brulé, M. Presse méd., xv, 641, 1907.
——— Arch. d. mal. d. cœur, i, 193, 1908.
——— Bull. et mém. Soc. méd. d. hôp. d. Paris, xxxiii, 480, 1912.

CHAPTER XL

DISEASES OF THE SPLEEN

FREDERICK FORCHHEIMER AND FRANK BILLINGS

REVISED BY GEORGE BLUMER

Movable Spleen.—Something may be tried in the way of causal therapy when splenoptosis is primarily due to chronic enlargement of the spleen, to be described hereafter. Otherwise the indication is to find a mode or modes of treatment by which the patient gets relief, temporary or permanent. First a well-fitting bandage should be tried; this should be elastic enough not to interfere with respiration, and must be applied so that it has a sufficient bony support by covering the lower part of the thorax. The lower edge of this kind of bandage should hold up the displaced organ. A pad is not necessary as a rule. It may be uncomfortable or even do harm, because, as there is no fixed base of support, the pad itself must necessarily make excursions. If a pad is necessary an abdominal bandage should be applied which does away with this difficulty. The bandage should cover the whole abdomen, be more or less rigid, and have fixed bases of support above and below. This form of treatment may be of some value when the abdominal walls have become weakened by repeated pregnancies, removal of fat, or reduction of the normal and intra-abdominal supports from any cause. Massage, electricity, and gymnastics are also recommended. It will be readily seen that they can be of value in very few cases. In enteroptosis due to pregnancy the milder cases may be benefited. The other forms are not affected by mechanical treatment alone. It is more rational to try to recover the intra-abdominal fat which has been lost for one reason or another and has acted as the internal support of the spleen. For this purpose rest after meals and superalimentation, especially with the fats and carbohydrates, should be ordered; the results of this simple treatment sometimes are astonishing.

This is one of the most important measures in enteroptosis, of which the floating spleen is usually one feature. In addition, postural treatment should be employed.

Either in general enteroptosis or in ptosis of the spleen alone the

patient's nervous condition must be considered. As long as they do not know their exact condition they may suffer some physical discomfort or even pain; as soon as they become acquainted with the whole state of affairs a nervous state is, as a rule, superadded which varies in intensity, not infrequently developing into neuroses or psychoses. The least that can be expected from the physician, under the circumstances, is that he be careful in the way in which he tells his patient of the nature of the ailment when he decides to tell.

It is especially in the neurotic cases that operation is indicated in enteroptosis. Three operations are performed: splenectomy, fixation of the spleen by suture, and the production of artificial adhesions by replacing the spleen and packing with gauze (Osler-Halsted). As to the results, it goes without saying that splenectomy cures, but there is a certain percentage of mortality. Of the results from the remaining two operations it may be safely said that they are valuable: for their temporary effects to the direct benefits of the operation; for their permanent effect to the operative results either because the organ has been held in place or that it has been reduced in size by having been held in place.

In many cases the cure is probably due to suggestion. I have seen patients operated upon for enteroptosis, I have seen them cured, and have examined them some time after the operation; the enteroptosis had recurred and many of them were not aware of it. It would be a cruel physician who would tell these patients without symptoms that the condition had returned. As yet neither surgical nor medical treatment is thoroughly satisfactory.

When, as is sometimes the case, there is torsion of the pedicle, surgical interference should take place as soon as the condition is suspected.

Rupture of the Spleen.—Rupture of the spleen may occur as the result of direct or indirect trauma, or may occur spontaneously. Spontaneous rupture only occurs in pathological spleens and particularly in the enlarged spleen of certain infectious diseases such as malaria, relapsing fever, typhus or typhoid fevers.

The symptoms are those of local disease, pain in the left upper quadrant radiating to the mid-abdomen or to the left axilla and shoulder, and associated with tenderness and muscle spasm over the organ, and in addition the symptoms and signs of progressive loss of blood.

The treatment is entirely surgical, for while there is evidence that spontaneous recovery can occur after small ruptures, this cannot be relied upon. The patient's only chance lies in early recognition and prompt laparotomy with splenectomy.

Infarct and Abscess of the Spleen.—In infarct of the spleen little can be done even when it is recognized. It is due either to embolism or thrombosis and the conditions which cause them, as a rule, preclude treatment. When the diagnosis is made and the causal condition is favorable,

operation should be done if there is reason to believe that the infarct is septic and suppuration is taking place. It would be folly to operate for a cachectic infarct.

Abscess of the spleen should always be treated surgically.

Chronic Enlargement of the Spleen.—The causal treatment of chronic enlargement of the spleen has been considered in connection with the infections, the leukemias, chronic myocardial insufficiency, diseases of the liver. There remains the treatment of chronic splenic enlargement as a symptom. It is useless to temporize with drugs in this condition. It is now well known that simple splenomegaly is the early stage of splenic anemia and that this, in turn, is followed by Banti's disease. Splenectomy is therefore indicated in these cases not merely for the relief of mechanical symptoms but as a preventive measure.

Thrombophlebitic Splenomegaly.—As Eppinger and Ranzi point out, there is a group of cases usually confused with splenic anemia, which should be differentiated. These are patients who have an enlarged passively congested spleen with compensatory circulation in the gastric and esophageal veins as the result of an obstructive thrombophlebitis of the splenic vein. These patients usually present themselves on account of severe hematemesis. They have an enlarged spleen and a history of an obscure febrile disorder lasting for some weeks, years preceding the vomiting of blood. Icterus and pruritus are absent, there is no urobilinuria, and no anemia except as a result of a recent hematemesis.

Treatment.—The treatment in these cases, as in splenic anemia, is splenectomy, but this should only be undertaken when the patient has suffered from hematemesis. The reason for this is that the thrombophlebitis of the splenic vein is accompanied by a severe inflammatory reaction, many adhesions are apt to be present and the removal of such spleens is much more difficult than the removal of the spleen of splenic anemia and accompanied by a much higher mortality.

Banti's Disease.—Banti reports 50 cases thoroughly studied, with the following results: The disease should be divided into three periods. (1) Enlargement of the spleen. Anemia less constant, slight, or occurring late. (2) Beginning congestion of the portal circulation. (3) Cirrhosis with ascites. Banti suspects that the disease is due to some infectious agent which lodges in the spleen; the anemia and cirrhosis are secondary to a toxin elaborated in the spleen and therefore he advocates early excising of the spleen as a cure. He thinks that if this be done in the first stage a large percentage of the cases can be cured.

The results of 36 cases operated upon are as follows: Four cases in the first stage: three cures after five, six, and fifteen years, respectively; 22 cases in the second stage: thirteen cures, some persisting seven, eight, and fourteen years; 10 cases in the third stage, four cures.

It is to be noted that some subjective cures result even in the third

stage and, inasmuch as many patients do not consult the physician until this stage is reached and hepatic cirrhosis is well marked, a combined operation, splenectomy and omentopexy (Talma-Morison operation), is often demanded.

Cysts of the Spleen.—These may be congenital (dermoid cyst), parasitic (echinococcus cyst), or acquired non-parasitic cysts, which may be either unilocular or multilocular.

The *symptoms* are entirely due to the dragging of the enlarged organ or to its pressure on neighboring viscera. The dragging of the organ results in soreness in the left upper abdomen and at times pain which may be referred to the left axilla and shoulder. Pressure is usually exerted on the stomach or intestines, causing either flatulence with indigestion and perhaps nausea and vomiting or else constipation.

The *treatment* is entirely surgical and the exact details vary with the individual case. In some patients the cyst is so situated that it may be removed or drained without removal of the spleen itself. In other patients the disease is so extensive that it is more desirable to perform a splenectomy.

Gaucher's Disease.—This is a condition originally described by Gaucher as primary endothelioma of the spleen. Subsequent studies, particularly those of Brill and Mandelbaum, have shown that the condition is not neoplastic and that the liver, lymph-nodes and bone marrow are also involved in the process. The lesion present in the different organs is an enormous hyperplasia of distinctive large cells with a peculiar cytoplasm and small nuclei.

The clinical characteristics of the disease are as follows: It is frequently a familial but not a hereditary disease, several cases occurring in sibs of the same generation. It is usually first recognized before the age of twelve. There are no subjective symptoms early in the disease, but as the spleen enlarges a sense of abdominal discomfort is often experienced and when it becomes very large there may be gastric or intestinal symptoms due to pressure. In the late stages hemorrhagic manifestations occur (epistaxis, gum bleeding, purpura, etc.).

Physical examination shows that there is a progressive enlargement of the spleen, and later of the liver, with brownish-yellow discoloration of the skin and peculiar yellowish wedge-shaped thickenings of the conjunctivæ. The blood shows definite leukopenia from the beginning and in the late stages a chloro-anemia may be present. The disease has little effect upon the general health, runs a protracted course and does not interfere with the ordinary activities of life. The patients usually die of some intercurrent infection.

Treatment.—Notwithstanding the fact that these patients are subjectively well, treatment is demanded for two reasons: first, because in

time pressure symptoms occur, and secondly, because these patients ultimately die of intercurrent disease at a comparatively early age.

Splenectomy is the only known treatment of value. Two of the 3 patients operated on by W. J. Mayo recovered after this operation. Inasmuch as the lesions are not confined to the spleen, the ultimate value of splenectomy may be questioned. It is to be noted, however, that in the interesting case reported by Keisman, not only did the liver enlargement disappear after the splenectomy, but the patient, an undeveloped girl of seventeen, menstruated and developed secondary sexual characteristics.

Primary Sarcoma of the Spleen.—Primary malignant growths of the spleen are decidedly rare and are usually sarcomata. Their early recognition is important because they are slow growing and metastasize late, so that the chances of recovery after early removal are excellent. The symptomatology is meager, as pain and blood changes are very inconstant, and the diagnosis must be made on the presence of a hard, usually nodular enlargement of the organ.

Treatment.—The treatment is prompt splenectomy, the results of which are usually excellent unless the growth is too far advanced.

CHAPTER XLI

DISEASES OF THE LYMPHATIC GLANDS

C. P. Howard

LYMPHADENITIS

Acute Lymphadenitis.—This is by far the most common affection of the lymph glands, resulting as it does from the entrance of bacteria or other foreign bodies by way of the afferent lymphatics in the localized form, or by the blood-stream in the generalized cases. In the local cases the various pyogenic organisms are usually present. The generalized form occurs in the following diseases: typhoid fever, measles, diphtheria, scarlet fever, variola, varicella and the glandular fever of Pfeiffer (infectious mononucleosis). In addition to the primary injury, the gland shows the usual tissue response, namely, lymphoid hyperplasia and the inflammatory reaction of a serous and cellular exudate.

Symptoms.—The symptoms are pain, swelling, tenderness of the affected glands, redness of the overlying skin and fluctuation if suppuration occurs. There is also invariably a general reaction indicated by fever and leukocytosis.

Treatment.—In the local group one first should remove the exciting cause; thus if the cervical group be involved the tonsils, pharynx, nose, mouth, teeth, ears and scalp should be carefully examined and all foci of infection excised or thoroughly drained. Locally, one should apply an ice-bag or cold compress. As soon as there is evidence of suppuration free surgical drainage, or, better still where possible, free excision of the involved glands should be instituted. The general health should be improved by providing an abundance of fresh air and nutritious food and in some cases by the exhibition of tonics of iron or arsenic. In the general lymphadenitis of the infectious diseases, one treats the disease itself and neglects the glands.

Chronic Lymphadenitis.—This may follow the acute variety or develop gradually without evidencing an acute stage. It occurs most frequently in the cervical glands of children harboring a low grade infection of the adenoids, tonsils, mouth or scalp. It is not uncommon in the

axillary group in women with a chronic mastitis. It is also well illustrated in the bronchial glands in cases of anthracosis, siderosis, etc. In these conditions the glands are seldom much enlarged, but are firm and reveal a thickened capsule and trabeculæ and either lymphoid hyperplasia or atrophy.

Treatment.—Treatment is usually of little avail except in a few cases where the focus of infection can be removed, as the tonsils, adenoids, carious teeth, pediculi, etc. The external application of lead acetate, lead iodid, potassium iodid and tincture of iodin was formerly urged, but is gradually falling into disuse, if not into disrepute, because of the danger of irritating the skin. X-rays cautiously applied may be tried, but as a general rule are unnecessary, indeed are inclined rather to aggravate the condition from the slight dermatitis they produce.

SPECIFIC LYMPHADENITIS

Under the heading of Specific Lymphadenitis should be included syphilis, gonorrhea and tuberculosis.

Syphilis

In the primary stage the "bubo" occurs four or five weeks after the infection; the glands of the groin (rarely those of the submaxillary or axillary region when the chancre is extragenital) gradually become enlarged to the size of a cherry but remain firm, non-adherent to the periglandular tissue and usually free from both pain and tenderness; if a mixed infection occur, an acute suppurative lymphadenitis may result. The course of the uncomplicated bubo is very indolent. In the secondary stage there is invariably a generalized hyperplasia of all the superficial and deep glands; the enlargement of the posterior cervical and epitrochlear group is always suggestive of syphilis. In the tertiary stage gummata not infrequently occur in the superficial glands or in the deep groups in association with disease of the liver, lungs and other organs. These gummatous tumors may become very large and produce pressure symptoms.

Treatment.—For the simple bubo no local treatment is necessary; when mixed infection is present an ice-bag and the application of tincture of iodin may suffice, though incision or even excision may be indicated. In the secondary stage no local treatment is necessary, but one, of course, should institute immediately courses of salvarsan or neosalvarsan or one of its American substitutes, as arsphenamin or diarsenol, and mercury (either hypodermically or by inunction) over a period of at least two years, even though the patient's serum Wassermann becomes negative before the expiration of this time.

Gonorrheal and Chancroidal Bubo

Enlargement of the inguinal group of glands is a constant manifestation of gonorrhea in the male, though distinctly less frequent in the female. The glands are only moderately enlarged, but are painful and tender, and, if secondarily involved by the pyogenic organisms, may suppurate. In the bubo of soft chancre there are often severe pain, chills and fever; the glands either unilaterally or bilaterally may enlarge to the size of a lemon or small orange and form a solid mass from the associated periadenitis. The skin over the bubo is reddened and edematous and fluctuation and external perforation may result in two or three weeks. Sometimes septicemia develops leading to a fatal termination.

Treatment.—The first indication is the treatment of the gonorrheal infection or of the chancroid. For the former injection or as some prefer, irrigations of the anterior urethra night and morning with various antiseptic solutions such as potassium permanganate in a dilution of 1: 8,000 or ammonium sulphichthylate 1:4,000. One must insist in care being taken to avoid washing the infection into the posterior urethra and the whole procedure must be gently carried out.

The chancroid should be cauterized with pure carbolic acid or by means of the Paquelin cautery under local or general anesthesia. If the ulcer is deep, wet dressings of corrosive sublimate (1:5,000) should be employed instead of cauterization; in addition night and morning applications of 50 per cent hydrogen dioxid are useful in cleaning up the surface of the ulcer. For the adenitis, the first essential is rest in bed for a period of several days. The ice-bag will be of distinct assistance; others prefer warm, moist dressings. Local applications of iodin and belladonna, lead acetate, etc., are much used in the form of moist dressings or ointments. Injection of the bubo with mercury benzoate, mercuric chlorid and carbolic acid is no longer practiced. When suppuration occurs free incision is necessary.

Tuberculosis

This is a very common affection of the lymph glands and manifests itself pathologically in one or more of the three following types: (1) miliary tubercles; (2) diffuse cellular hyperplasia; and (3) rapid caseation and softening. Various groups of glands are especially exposed to infection, namely the cervical, the bronchial and the mesenteric, draining as they do the three usual portals of entry of the tubercle bacillus. Involvement of the axillary and inguinal groups is comparatively rare. Generalized tuberculous lymphadenitis may occur but can only be distinguished from Hodgkin's disease by a careful histological study.

The symptoms of tuberculosis of the glands vary somewhat according

to the locality of the group involved. In the *cervical cases* the submaxillary glands are usually first enlarged and a little tender and gradually the upper nodes of one or both anterior cervical groups become affected. They slowly enlarge to the size of an almond, become adherent to the periglandular tissue and eventually to the overlying skin. One or more of them suppurates and points externally leaving a sinus that heals very slowly. There are usually fever, slight leukocytosis, anemia and varying degrees of cachexia. In the *tracheobronchial* group there may be no symptoms, but if the glands are much enlarged there may result a brassy cough and other pressure symptoms as well as the general ones of fever, cachexia and anorexia. In the *mesenteric cases* the abdomen becomes distended; there is a constant diarrhea, some fever and a marked wasting of the body tissues, well designated by the old term "tabes mesenterica."

Treatment.—We must consider (1) general, (2) specific, and (3) local measures.

General.—The general measures, as in tuberculosis elsewhere, consist of a suitable climate, abundance of fresh air and sunshine, good nourishing food, but not overfeeding, and the rational administration of tonics for the appetite, iron and arsenic when there is anemia and in poorly nourished rickety children, possibly cod-liver oil if it does not interfere with the appetite and digestion. The ideal climate is usually obtained in high altitudes with a dry atmosphere. Massage and salt baths may also be called into requisition to aid the general resistance.

Specific Treatment.—Tuberculin is indicated in cases in which the disease is strictly localized and more particularly to the cervical group. One may use either Koch's old tuberculin (O. T.) or the bacillary emulsion (B. E.) or the filtrate (B. F.) singly or combined. The dosage must be determined for each case, the object being to produce a slight local reaction, but to fall short of a general one. If old tuberculin is used one should begin with the hypodermic administration of 0.0000001 gm. and repeat in seven to ten days before cautiously increasing the dose by about one-tenth; this minute dose is obtained by diluting 1 c.c. of the tuberculin which contains 1 gm. Local reactions in spite of every precaution may become quite distressing and indicate a discontinuance of the tuberculin for a time and the use of a smaller dose in the future. The emulsion is measured in terms of bacillus substance, 1 c.c. being the equivalent of 5 mg. of solid substance; the initial average dose is 0.0000001 gm.; it should be increased with the same caution. The initial dose of the Bouillon filtrate (B. F.) is the same as that of Koch's old tuberculin. Tuberculosis vaccines made from attenuated cultures of the human, bovine or avian strain have also been tried.

Local Treatment.—This, of course, is possible only where the superficial glands are involved, particularly the cervical and axillary or inguinal. Some (Floyd) urge the removal of the tonsils as a preliminary

procedure in the treatment of cervical adenitis, as in at least 5 per cent, probably in more of these cases, the tonsils are the seat of tuberculous foci. Care must be exercised as in one case of the author's (C. P. H.), a tonsillectomy was followed by a generalization of the tuberculosis process and the rapid appearance of a tuberculous synovitis of the hip, a tuberculous mastoiditis and finally a meningitis with death.

There is still some diversity of opinion as to whether or not a thorough dissection of the neck should be attempted. My own opinion is strongly against prolonged operations in cases of tuberculous adenitis because the surgeon rarely, if ever, removes all the infected tissue and the patient is exposed to an acute respiratory infection which may eventually light up a dormant pulmonary tuberculosis. However, all must agree that once a gland breaks down the abscess so formed must be incised and drained by proper surgical procedures.

The use of the Roentgen ray was formerly objected to on the ground, according to Warthin, that: "Too many dangers attend the prolonged and vigorous irradiation necessary to reduce the size of the enlarged nodes. Moreover, in glands so treated an active eruption of miliary tubercles may occur at the periphery of the caseous areas." With the improvement in X-ray technic, however, many writers have reported encouraging results, notably Boggs, Carter, Edling and Ratera. Carter believes in a softer X-ray than do many and uses a 2 mm. aluminum filter, a 5-inch spark gap, 4 m.a. and five-minute exposures; he advises a treatment every five to seven days until the glands show perceptible decrease in size, when the interval may be lengthened to two weeks. Carter found that eight to ten treatments usually sufficed to reduce the glands to normal size, but he recommends as desirable twenty-four treatments over a period of ten months. Others use stronger doses of a more penetrating ray, but with more filtration. Edling is quoted by Floyd to the effect that of 206 cases treated by the X-ray, 75 per cent resulted in complete cure. Boggs is more optimistic and is convinced that radium and the Roentgen rays will cure 90 per cent. The writer always submits his cases of tuberculous adenitis to the Roentgen ray laboratory and so far the results seem to justify the practice.

STATUS LYMPHATICUS

While this condition may be discussed at greater length in the section on Diseases of the Thymus Gland, we consider it merits at least a passing mention in the orderly consideration of hyperplasia of the lymphatic glands. According to Douglas Symmers there are two types: (*a*) status lymphaticus, (*b*) recessive status lymphaticus. In the former there are well-developed changes in the lymphoid tissue at an age when these struc-

tures are active; in the latter there are atrophic changes in the lymphoid structures varying with the time of the involution, "the other anatomic anomalies remaining of course unchanged. The lymph-nodes show a peculiar and characteristic change in the form of a necrosis of the germinal areas attended by extensive disintegration of cells and the discharge of nuclear dust in the intercellular spaces" (Symmers).

Symptoms.—The symptoms are often lacking. The child may appear somewhat flabby and anemic and reveal a tendency to mouth breathing and a susceptibility to nasal catarrh and other acute infections. In the more advanced cases stridor, thymic asthma, or even sudden death may occur. Often the death follows some trivial procedure as bathing or sometimes occurs during a minor operation such as puncture of the chest or the extraction of a tooth.

On examination one notes a slender physique inclined to the feminine type; a soft delicate skin; a scanty growth of hair; poorly developed genitalia, enlarged cervical and axillary glands and enlargement of the thymus to percussion and in the skiagram. Of medicolegal interest is a tendency to cerebral hemorrhage occurring either spontaneously or following slight trauma.

Treatment.—This consists first of palliative, and second, operative treatment for the thymic asthma.

Palliative Treatment.—A quiet out-of-door life in an equable climate is the ideal. In general it is well to reduce to the minimum the sugar and starch of the diet, substituting for them skim milk, eggs, meat, green vegetables and fruits. Iron and arsenic will serve as general tonics. Treatment for syphilis or rickets should be carried out, if indicated. In addition one should teach the child to hold the head erect and if necessary provide a special orthopedic collar. The head should never be thrown far backward. The patient should be kept as quiet as possible and attacks of crying or other strong emotional disturbance should be avoided.

Surgical operations, especially those requiring anesthesia, should be undertaken with great caution, and always with a tracheotomy set ready for an emergency. It has been suggested that a course of radiation to the thymic region should proceed even a minor operation in this group of cases. Very warm or very cold baths should be proscribed, and swimming, or even bathing, should be forbidden. All possible measures should be enforced to protect the child from acute infections of the upper respiratory tract and especially from the acute exanthemata.

Curative Treatment.—In cases of thymic asthma or stridor, more radical treatment will be necessary. X-rays should certainly be given a trial, as they have a peculiar selective action on lymphoid tissues and have been shown, both experimentally and clinically, capable of reducing the size of the thymus. The usual cautious technic must be enforced, both as to dosage and filtration. Cozzolino reports 8 cases successfully treated by

this means. Meyer is very enthuiastic after treating 50 cases of enlarged or persistent thymus; he believes that the selection of penetration should be such that the best possible absorption rate be brought to bear on the lesion and the adjustment of milliamperes and distance such that the treatment be not excessively long.

Intubation by means of a long tube reaching to the bifurcation of the trachea has been used by Marfan in tiding the patient over a severe paroxysm.

Thymectomy or the surgical removal of the thymus has been successfully performed by several of the best known thoracic surgeons both in Europe and America.

LYMPHOCYTIC LEUKEMIA

While lymphocytic leukemia is admitted to be a clinical variety of a hyperplasia of the hematopoietic system associated with a permanent increase in the leukocytes of the blood, it must necessarily be mentioned in this chapter as well as in that on Disease of the Blood. It may run either an acute or a chronic course.

Acute Form.—The acute variety "is an acute febrile disease characterized by the presence in the peripheral blood of a cell morphologically resembling the small lymphocyte in relative preponderance" (Panton, Tidy and Pearson). While the glands of the neck, axillæ and groins may become somewhat enlarged, death usually occurs before any marked adenitis has had time to develop. The spleen, though rarely much enlarged, is usually palpable. An acute tonsillitis, ulcerative angina, stomatitis with hemorrhages from the gums, generalized purpura, fever and a rapidly progressive anemia are the main clinical features. The characteristic sign is a leukocytosis which is usually of a moderate degree (22,000 on an average) but which may occasionally vary between 100,000 and 200,000 per c.mm. or even higher. The predominating leukocyte was formerly considered to be the large lymphocyte, but with modern methods of staining the small lymphocyte is now shown to be the overwhelmingly predominant cell. This acute course is more common in children and young adults up to the third decade.

Chronic Form.—The chronic variety is, contrary to former teaching, the least common of all varieties of leukemia. It is, however, the most chronic in its course and may last from four to ten years. It is essentially a disease of later life and occurs usually in the fifth and sixth decades. As a rule, the general health is good and the patient consults his physician largely because of the inconvenience of the enlarged glands. The lymphatic glands of every region of the body are affected, sometimes to such a degree as to interfere with the movements of the arms and legs. The mesenteric and retroperitoneal groups may form big tumors that interfere with the efficiency of the gastro-intestinal tract. The glands are

globular or ovoid in shape and remain perfectly discrete; they are soft, but never break down. The spleen is rarely very large. The leukocytes are usually much increased and vary from 100,000 to 150,000 and occasionally reach even to 800,000. Cabot found in his series an average of 141,000 per c.mm. The predominating cell is the small lymphocyte which forms from 90 per cent to 99 per cent of the total leukocytes.

Treatment.—In the acute variety one is practically helpless and all attempts to stem the progress of this terrible disease are in vain. The most that can be done is to make the patient comfortable by providing a bland soft or liquid diet, an ice-bag to the head, and tepid sponges every four hours, which will help to control the fever. For the bleeding from the gums, painting with various astringents, adrenalin and cocain, and touching the bleeding points with a pencil of silver nitrate may be tried. The anterior and posterior nares may require packing by a rhinologist. The subcutaneous administration of horse serum (10 c.c.) or of whole citrated or defibrinated human blood may temporarily check the hemorrhagic tendency. Thromboplastin, calcium lactate and other supposed coagulants are in our experience useless. Blood transfusion may postpone the end by a day or two, but the patient will continue to lose blood from the various mucous membranes in spite of every means yet devised.

While the chronic cases require a less active attack, the means at our disposal are almost as valueless. Osler tersely puts it: "Fresh air, good diet and abstention from mental worry and care are the important general indications. The indicatio morbi cannot be met." Some advise removal of infected tonsils and teeth in the belief that the disease is of infectious origin. Arsenic in any form seems to exert some slight influence on the course of the disease; it is more usually exhibited as Fowler's solution beginning at 3 drops and gradually increasing to 10 or 15 three times a day; some prefer the subcutaneous or intravenous administration of atoxyl (gr. i) or cacodylate of sodium (gr. 1½) or arsphenamin (0.6 gm.). Iron in the form of Blaud's pills may help to counteract the anemia. Quinin in large doses and phosphorus have been used by some clinicians, but the general experience is that these drugs are of less service than arsenic. Some have tried nucleinic acid, sodium cinnamate and various stock vaccines in the forlorn hope of obtaining an increase in the polynuclear cells, but in vain. Benzol is of no assistance in this type of leukemia as it has no antagonistic action to the lymphoid tissues. However, benzyl benzoate in the form of a 20 per cent alcoholic solution in doses of 10 drops three times a day is reported by Haughwout and Azuzano to have produced a marked improvement in the general condition, a temporary reduction in the white count and moderate dimunition in the size of the spleen and liver in a case of chronic lymphocytic leukemia. This drug is worthy of further trial as it produces no untoward or disagreeable symptoms according to Macht.

Colloidal Gold.—Colloidal gold has been given intramuscularly in 5 c.c. doses by Cawadias and Monphrrato (quoted by Ordway) to a case of chronic lymphocytic leukemia with a resulting fall in the leukocytes from 103,000 to 62,000.

Radiotherapy—Radiation by means of radium and the Roentgen tube has undoubtedly a beneficial, though alas but a temporary effect on the glands and blood picture in lymphocytic leukemia; the results are perhaps not quite as striking as in the myelocytic variety.

If *radium* be used the usual dosage for each gland area is 60 to 100 mg. of the radium element or millicuries of emanation; this dose may be repeated in four to six weeks. A filter of lead 2 to 3 mm. in thickness must be used to absorb the alpha and soft beta rays. The radium applicator which usually consists of wood lined with lead is wrapped in gauze and held in place by adhesive straps or a firm bandage.

Mesothorium and thorium-X have also been used to induce remissions in the chronic type. The technic of their application is very similar to that of radium. In addition, Falta and his associates have produced remissions in a few cases of leukemia by intravenous or intramuscular injection of a normal saline solution containing the emanations of thorium-X. There is, however, some risk associated with this drug and several fatalities have occurred.

If *X-rays* are to be tried one must use the so-called "cross-fire" method of Dominici, the aim of which is "to concentrate as much of the action of the rays as possible in the deep-seated lesion with the least possible injury to the overlying skin." In other words, the gland region is exposed anteriorly, posteriorly and laterally. One must, of course, use screens and filters of aluminum (1 to 3 mm.) and sole leather to protect the skin from the action of the less penetrating rays which would otherwise be absorbed by the superficial tissues. A hard tube with a high degree of vacuum and an apparatus of high voltage will give the most penetrating ray. The treatment may be repeated in two to three weeks. Occasionally untoward results follow both radium and X-rays, as dermatitis, erythema and burns of the skin and such toxic symptoms as headache and nausea.

Radical Surgery.—Radical surgery has been advised by some and may be justified in the exceptional case. In general, however, surgery offers as little as medical treatment in this disease.

Symptomatic treatment is necessary for certain of the complications, especially of the acute group. The oral sepsis calls for the frequent use of cleansing and astringent mouth washes. Great caution must be exercised in the extraction of teeth because of the danger of inducing uncontrollable hemorrhage from the gums. When hemorrhages do occur, blood transfusion and the local and subcutaneous use of serum or of thromboplastin are indicated.

ALEUKEMIA LYMPHATICA

Under this caption we would include cases of chronic progressive enlargement of the lymph glands without a leukemic blood picture or the histological gland changes of Hodgkin's disease, tuberculosis or lymphosarcoma. They are probably cases of chronic lymphocytic leukemia in an aleukemic stage which may occur as the result of an intercurrent infection or some physical trauma. This aleukemic stage may be purely temporary or it may be permanent over a period of years of observation. The blood smear, however, usually shows a relative lymphemia varying from 30 per cent up to 50 per cent or more; the neutrophil count is low, while the large mononuclear and transitional cells may reach as high as 8 to 10 per cent. It is true that patients with this disease rarely live out their natural expectancy and seem especially susceptible to acute infections, which may terminate the disease before the leukemic blood picture has had time to make its appearance. Be this as it may, the treatment is as unsatisfactory as that of chronic lymphocytic leukemia, but in general may be directed along similar lines.

HODGKIN'S DISEASE

By Hodgkin's disease we mean "an affection characterized by a progressive enlargement of the lymph glands (of specific character), a moderate anemia, a terminal fever and a fatal course" (Bunting).

Thanks to the pioneer work of Dorothy Reed, Longcope, Andrews, Bunting and others, malignant granuloma rests upon a firm pathological and histological foundation. The scope of this article does not permit a review of the various theories that have been advanced concerning the pathology and the pathogenesis of the disease. Suffice it to state categorically that the gland changes are neither those of tuberculosis nor of a neoplasm. They are rather those of some inflammatory process characterized by a "proliferation of the endothelial and reticular cells, with the formation of lymphoid cells of uniform size and shape and characteristic giant cells, the so-called lymphadenoma cells, containing four or more nuclei. Eosinophils are always present and proliferation of the stroma leads to fibrosis of the gland" (Osler).

Symptoms.—While the superficial glands of the neck are most frequently involved, any or all the groups of superficial or deep glands may be involved. As a rule, the glands tend to remain discrete, yet sometimes the capsule may be infiltrated and the adjacent tissues involved; further they may erode the sternum or exert pressure on the ureters, the lumbar and sacral nerves, the iliac veins or even the thoracic duct. The

symptoms are often ushered in by tonsillitis or other infection of the upper respiratory tract. Sooner or later the cervical glands of one or both sides become enlarged and months or years later the axillary, mediastinal abdominal and ilio-inguinal groups are affected. The spleen is invariably palpable, but rarely reaches the size of the leukemic spleen, except in the rare splenomegalic type of the disease. Cough, dyspnea and cyanosis result from pressure on the mediastinal contents. There is usually a moderate fever, sometimes continuous, sometimes irregular or intermittent, and sometimes of the relapsing type described first by Murchison and later known as the Pel-Ebstein syndrome. The skin is usually bronzed and there may be intense itching. Cachexia is eventually marked. The blood shows in the early stages a slight anemia which later may become marked and associated with normoblasts, but is always of the secondary type. The leukocytes in the early stages are usually within normal limits or, at the most, slightly above normal; at first there is a slight relative lymphocytosis which gradually subsides. The eosinophils show a slight but definite increase and in some cases may be markedly increased, even to as high as 36 per cent according to Bunting. There is a definite increase in the large mononuclear and transitional cells to about 10 per cent throughout the course of the disease (Bunting). Blood-platelets are increased in number and one often sees unusually large forms. Later in the disease there is a definite leukocytosis, often as high as 20,000 per c.mm. with an increase in the polymorphonuclear cells to 80 per cent or 90 per cent.

Diagnosis.—The diagnosis should always be confirmed by the histological study of an excised gland, which can be readily obtained under local anesthesia.

Treatment.—Hygiene, arsenical drugs, surgery and radiation with the Roentgen tube or radium are our main lines of therapy. Under hygiene should be included fresh air and sunshine, good nourishing food and both physical and mental rest. Mineral baths have seemed beneficial in some cases, according to G. R. Murray.

Medicinal Therapy.—Fowler's solution in gradually increasing dosage certainly aids in combating the anemia and may result in a temporary decrease in the size of the glands. Phosphorus, quinin, and iron in the form of Blaud's pills are useful tonics. Iodin, either in the form of the tincture or as potassium iodid, has no influence upon the progress of the disease and more often exerts a depressing effect upon the general condition of the patient. Various extracts of the lymphatic glands, thymus and bone marrow have proved worthless.

Vaccines.—Vaccine therapy has had its advocates and shortly after Bunting and Yates first isolated a diphtheroid bacillus from the glands of Hodgkin's disease, an autogenous diphtheroid vaccine was enthusiastically employed by many physicians (among others Billings and Rose-

now) but this vaccine has long since been discarded like many of its predecessors.

Local Measures.—Local measures, as massage, hot and cold fomentations, the ice-bag and painting with tincture of iodin are of little or no avail in reducing the size of the glands. Formerly various solutions, as arsenic, iodin, potassium iodid, silver nitrate, carbolic acid and chromic acid were injected into the substance of the gland but resulted in more harm than good.

Surgery.—In the early stages of the disease when the process is confined to the neck and the mediastinal glands are not involved, a thorough dissection of the glands is worthy of trial. Sir William Gowers advised against operation when the red cells were less than three millions. The presence of a high fever would indicate, at least, a postponement of operation. Murray believes that a marked leukocytosis is also unfavorable to operation. The technical difficulties are often very great, and one rarely eradicates even locally the disease process. Bunting and Yates, who are the most enthusiastic advocates of the surgical method, urge that, prior to the removal of the affected lymphatic glands, all foci of infection in the mouth and throat, such as diseased tonsils, infected sinuses and abscessed teeth, should be taken care of. In the splenomegalic type of the disease, splenectomy seems justifiable and in one case of the author's prolonged life and even bodily activities for several years.

Radiation.—Radium and the X-rays are of undoubted temporary benefit, though they do not cure the disease. On several occasions in our own medical clinic, we have seen a critically ill patient leave the hospital in comparative well-being after a course of X-ray treatment to the affected regions. Radium may be tried in cases with very large local gland masses and in the splenomegalic type of the disease. It must be confessed, however, that we, like other clinicians, have found some cases that do not respond with such alacrity and particularly is this true of the more fibroid type of glands. In general we prefer the X-ray radiation and would particularly commend the technic employed by Allen in the University Hospital at Iowa City. Briefly, this consists of a 9 and 1-inch spark gap, 5 m.a. current, an anode skin distance of 15 inches and a filter of 4 mm. of aluminum and one layer of sole leather. The time of exposure varies from five to twenty minutes over a period of from five to fifteen days, depending upon the condition of the patient and the response of the glandular enlargement. Longcope advises a somewhat similar technic. The treatment should always be controlled by the blood count and, when the leukocytes fall to 2,000 per c.mm., the X-rays should be temporarily discontinued until such time as the white cells return to normal. Occasionally the patient complains of malaise, headache, nausea, vomiting and fever, especially when the abdominal glands or spleen are exposed. Schirmer, Pancoast and more recently Levin and Bowing have

reported very encouraging, though, of course, purely temporary results from X-ray radiation.

When radium is used one can follow the technic employed by Wood at the Crocker Research Laboratories: "The radium, screened with 2 mm. of lead and 3 to 4 cm. of gauze is fastened over the enlarged nodes for periods that vary according to the quantity of radium used." It is considered safe to leave 100 to 200 mg. screened in the above manner on the lymph-nodes for twenty-four hours. Bowing, at the Mayo Clinic, recommends that radium be used for the superficial glands and deep X-ray therapy for the thoracic and abdominal groups. He uses 1,000 mg. hours of radium applied with the usual screening to areas 3 cm. by 4 cm. over the glands involved, the number of areas depending upon the extent of the involvement.

LYMPHOSARCOMA

Lymphosarcoma can be defined in the sense of Kundrat as "a growth of lymphoid tissue somewhat more restricted locally than in Hodgkin's disease or pseudoleukemia, but with greater invasive tendencies, suggesting sarcoma, but without marked evidence, at least of metastasis by the blood-stream." This concise definition of Bunting tells nearly the whole story of our knowledge of this pathological entity.

Kundrat and Bunting, among others, believe that it is closely related to Hodgkin's disease and pseudoleukemia. MacCallum insists that it is sharply differentiated from Hodgkin's. The growth starts simultaneously in a group of the superficial or the deep glands, or even of the lymphoid structures of the intestine. The mediastinum is a very frequent site of primary involvement, whence the growth invades the pericardium and the pleura; it tends to spread in the loose tissues and in a film or plate form over serous surfaces. Histologically, the growths are characterized by a reticular tissue and a large type of lymphoid cells; at the margin of these tumors infiltration of the surrounding tissues occurs, but without destruction of the tissue elements.

The symptoms depend, of course, upon the site of the involvement. If the cervical glands are involved, the clinical picture suggests Hodgkin's disease except for the more rapid involvement of the periglandular structures. In the mediastinal cases the symptoms are those of a mediastinal tumor, namely, cough, dyspnea, cyanosis, dysphagia, an increased area of dulness over the manubrium and a widening of the mediastinal shadow in the skiagram. In the abdominal cases, the symptoms may suggest an obscure infection or atypical typhoid fever.

The blood picture is not characteristic, but usually reveals a high percentage of large mononuclear and transitional cells and a diminished num-

ber of lymphocytes. The diagnosis can often only be made in the operating or postmortem room. It runs a more rapid course than Hodgkin's disease.

Treatment.—What has been said of the treatment of Hodgkin's disease applies to lymphosarcoma, especially in regard to the early surgical removal of the superficial gland lesions, followed by radium and X-ray therapy. Personally we have never seen a definite temporary response to any therapeutic procedure in this disease. However, Levin states "that the ultimate results are possibly better in lymphosarcoma than Hodgkin's, since, in the former, generalization does not take place as readily as in the latter." He further has noted that radiation of one group of glands may be followed by a decrease in size of another group. He expresses no opinion of his own as to what the mechanism of this influence is, but states that the theory of a liberation of specific enzymes from the disintegrating lymphocytes, however plausible it may be, is not yet proved.

MALIGNANT NEOPLASMS

Round cell and spindle-cell *sarcomata* may develop in the lymph glands and invade the surrounding tissues and develop metastases just as sarcoma of other organs. The treatment is entirely surgical, followed by radiation.

Bunting states that *endotheliomata* are more common than true sarcomata. Ewing recognizes a diffuse, a perivascular and an alveolar type of growth. They produce only occasional visceral metastases and spread by the lymphoid tissues. Symptomatically these cases cannot be distinguished from the Hodgkin's disease group. Their treatment is the same.

REFERENCES

Billings, F., and Rosenow, E. C. The Etiology and Vaccine Treatment of Hodgkin's Disease, Journ. Am. Med. Ass., lxi, 2122-2123, 1913.

Boggs, R. H. The Treatment of Tuberculosis Adenitis by Roentgen Rays and Radium. Am. Journ. Med. Sc., clxii, 90-95, 1921.

Bowing, H. B. Value of Radium and X-ray Therapy in Hodgkin's Disease, Journ. Radiol., ii, 20-24, 1921.

Bunting, C. H. Diseases of the Lymph Glands, Nelson's Loose-Leaf Medicine, iii, 347-368, 1920.

Cabot, R. C. Anæmia, Chlorosis and Leukæmia, Osler and McCrae's System of Medicine, iv, 653-676, 1908.

Carter, L. J. The Treatment of Tuberculosus Cervical Adenitis. Journ. Radiol., ii, 22-29, 1921.

Cozzolino, O. Stridore timico e stridori pseudotimici, Pediatria, xxix, 729, 1921.

Ewing, J. Endothelioma of Lymph Nodes, Journ. Med. Res., xxviii, 1-39, 1913.

Floyd, C. Tuberculosis of the Lymphatic Glands, Nelson's Loose-Leaf Medicine, iii, 369-381, 1920.

Haughwout, F. G., and Azuzano, M. A. Notes on the Treatment of a Case of Lymphatic Leukemia with Benzyl Benzoate, N. Y. Med. Journ., cx, 180-183, 1919.

Levin, I. Action of Radium and Roentgen Rays on Normal and Diseased Lymphoid Tissue, Journ. Am. Med. Ass., lxxvii, 930-933, 1921.

Longcope, W. T., and McAlpin, K. R. Hodgkin's Disease, Oxford Medicine, iv, 1-43, 1920.

Meyer, W. H. Roentgen Therapy of Intrathoracic Lesions with Special Reference to Status Thymus Lymphaticus, Arch. Pediat., xxxviii, 572-583, 1921.

Murray, G. R. Lymphadenoma, Allbutt and Rolleston System of Medicine, iv (Part 1), 459-481, 1908.

Ordway, T., and Gorham, L. W. Leukemia, Oxford Medicine, ii, 681-762, 1920.

Osler, W., and McCrae, T. The Principles and Practice of Medicine, D. Appleton & Co., 738-742, 1921.

Panton, P. N., Tidy, H. L., Pearson, G. H. The Leukemias: An Analysis of Fifty-nine Consecutive Cases, Quart. Journ. Med., vii, 340-367, 1914.

Symmers, D. Status Lymphaticus, Nelson's Loose-Leaf Medicine, iii, 319-325, 1920.

Warthin, A. S. Diseases of the Lymphatic Glands, Osler and McCrae's System of Medicine, iv, 808-831, 1908.

Yates, J. L., and Bunting, C. H. Results of Treatment in Hodgkin's Disease, Journ. Am. Med. Ass., lxviii, 747-751, 1917.

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